Supreme Court, U.S.
FILED

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No. OFFICE OF THE CLERK

In the
Supreme Court of the United States

VANDERBILT UNIVERSITY,
Petitioner,

v.

ICOS CORPORATION,
Respondent.

On Petition for Writ of Certiorari to the United States Court of Appeals for the Federal Circuit

PETITION FOR WRIT OF CERTIORARI

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September 21, 2010

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QUESTIONS PRESENTED

1. Whether the Court of Appeals can impose a clear and convincing evidence burden on a statutory civil action where there is no indication in the statute or its legislative history that Congress intended a burden of proof higher than the preponderance of evidence standard normally imposed upon civil actions.

2. Whether the Court of Appeals' failure to remand the case to the District Court conflicts with the United States Supreme Court's decision in *Pullman Standard v. Swint*, 456 U.S. 273 (1982).

RULE 14.1(b) STATEMENT

A list of all parties to the proceeding in the Court whose judgment is the subject of this petition is as follows:

The Petitioner, and the Plaintiff-Appellant below, is Vanderbilt University.

The Respondent, and the Defendant-Appellee below, is ICOS Corporation.

There were no additional parties to the proceedings below.

RULE 29.6 STATEMENT

Vanderbilt University is an independent, privately supported university incorporated on August 6, 1872 under the laws of the State of Tennessee with its principal place of business located at 305 Kirkland Hall, Nashville, Tennessee 37240. Vanderbilt University has no parent corporations and there is no publicly held company owning ten percent (10%) or more of Vanderbilt University's stock.

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PETITION FOR WRIT OF CERTIORARI

The Petitioner, Vanderbilt University, respectfully petitions for a writ of certiorari to review the ruling of the United States Court of Appeals for the Federal Circuit.

OPINIONS BELOW

The opinion of the Court of Appeals is published at 601 F.3d 1297 (App. at 1a-30a). A petition for rehearing and petition for rehearing *en banc* was denied without opinion on June 23, 2010. (App. at 86a).

The opinion of the United States District Court for the District of Delaware is published at 594 F. Supp. 2d. 482 (App. at 31a-83a).

JURISDICTION

The United States Court of Appeals for the Federal Circuit issued its opinion on April 7, 2010 (App. at 1a-30a), and its order denying rehearing and rehearing *en banc* was entered on June 23, 2010. (App. at 86a). The jurisdiction of this Court is invoked under 28 U.S.C. §1254(1).

RELEVANT STATUTORY PROVISIONS

35 U.S.C. §116. Inventors

When an invention is made by two or more persons jointly, they shall apply for patent jointly and each make the required oath, except as otherwise provided in this title. Inventors may apply for a patent jointly even though (1) they did not physically work together or at the same time, (2) each did not make the same type or amount of contribution, or (3) each did not make a contribution to the subject matter of each claim of the patent.

If a joint inventor refuses to join in an application for patent or cannot be found or reached after diligent effort, the application may be made by the other inventor on behalf of himself and the omitted inventor. The Director, on proof of the pertinent facts and after such notice to the omitted inventor as he prescribes, may grant a patent to the inventor making the application, subject to the same rights which the omitted inventor would have had if he had been joined. The omitted inventor may subsequently join in the application.

Whenever through error a person is named in an application for patent as the inventor, or through error an inventor is not named in an application, and such error arose without any deceptive intention on his part, the Director

may permit the application to be amended accordingly, under such terms as he prescribes.

35 U.S.C. §256. Correction of named inventor

Whenever through error a person is named in an issued patent as the inventor, or through error an inventor is not named in an issued patent and such error arose without any deceptive intention on his part, the Director may, on application of all of the parties and assignees, with proof of facts and such other requirements as may be imposed, issue a certificate correcting such error.

The error of omitting inventors or naming persons who are not inventors shall not invalidate the patent in which such error occurred if it can be corrected as provided in this section. The court before which such matter is called in question may order correction of the patent on notice and hearing of all parties concerned and the Director shall issue a certificate accordingly.

STATEMENT OF THE CASE

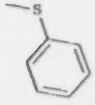
This petition seeks review of a decision of the United States Court of Appeals for the Federal Circuit (the "Court of Appeals") to impose a clear and convincing evidence burden of proof on a civil action under 35 U.S.C. §256 where neither the statute nor its legislative history indicate that Congress intended that

the burden of proof be higher than the preponderance of evidence standard normally imposed upon civil actions. This petition also seeks review of the Court of Appeal's decision not to remand the Petitioner's 35 U.S.C. §256 claim to the District Court for consideration of the evidence under the appropriate legal standard for determining joint inventor status under 35 U.S.C. §116, after the Court of Appeals correctly held that the District Court had applied an incorrect standard.

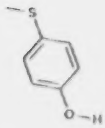
Factual Background. Petitioner Vanderbilt University ("Vanderbilt") alleges that three of its faculty scientists made substantial contributions to the conception of chemical compounds claimed in U.S. Patents Nos. 5,859,006 and 6,140,329 (the "Patents") such that, under the standard established in 35 U.S.C. §116, those scientists should have been named joint inventors on those patents. The compounds claimed in the Patents function as inhibitors of phosphodiesterase V ("PDE V"), an enzyme found in smooth muscle tissue that moderates the process through which such tissue relaxes. In the case of vascular smooth muscle tissue such relaxation results in dilation and increased blood flow. (App. at 34a, ¶4). PDE V inhibitors have been shown to be effective in treating erectile dysfunction ("ED") and the compounds claimed in the Patents include the active ingredient in the prescription ED medication *Cialis*®. (App. at 35a-36a, ¶7).

Vanderbilt Scientists, Jackie Corbin, PhD and Sharron Francis, PhD, were pioneers in the study of smooth muscle relaxation and are credited with having been the first to identify the PDE V enzyme. (App. at

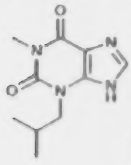
3a; 39a, ¶13). In November 1991 Drs. Corbin and Francis, working with by Sekhar Konjeti, PhD, developed a theory for designing more potent PDE V inhibitors. Using that theory, they created a new PDE V inhibitor by attaching an electron donating hydroxy group
(OH) at the 4 position on a bulky phenyl thio group



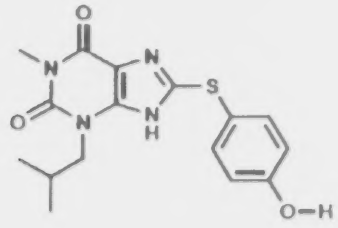
and attaching the resulting 4-hydroxy phenylthio



to the 8 position on an existing PDE V inhibitor known as IBMX



to create 8-(4-hydroxy phenylthio)-IBMX:

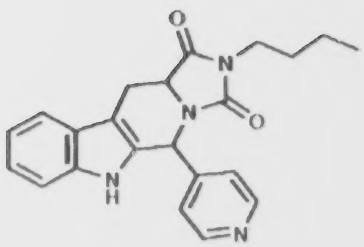


8 (4 OH PT) IBMX

(App. at 52a-53a, ¶41). It is undisputed that, at the time, this was a novel PDE V inhibitor and that nothing in the published state of the art described a PDE V inhibitor with the unique structure outlined above in red.

In late December 1991, Dr. Corbin spoke with Dr. Barry Ross, head of a group of scientists at Glaxo working on the development of new drugs to treat cardiovascular disease, about obtaining a research grant from Glaxo to fund, among other things, Vanderbilt's work on designing new PDE V inhibitors. (App. at 54a, ¶44). As a result of the conversation Dr. Ross asked Dr. Corbin to describe the work in a letter and planned a trip from his home in England to Nashville to hear more about Dr. Corbin's work. (App. at 57a, ¶49). Without describing the modifications, Dr. Corbin's January 3, 1992 letter explained how Vanderbilt's modifications to IBMX had increased by 160 fold the compound's potency as a PDE V inhibitor. (App. at 55a-56a, ¶46). It was undisputed that such a dramatic increase in potency would have been considered significant to scientists working in the field. (App. at 80a-81a, ¶89).

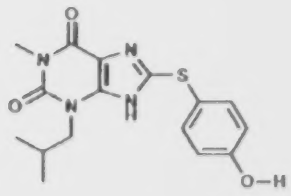
During his visit to Nashville Dr. Ross asked Dr. Corbin to provide more detail about the PDE V inhibitor that he and his colleagues had developed. On February 24, 1992, Dr. Corbin sent such detail to Dr. Ross in the form of a formal research proposal. (App. at 57a, ¶50). On April 8, 1992 Dr. Ross sent copies of the 1992 Research Proposal to six Glaxo scientists, including Dr. Richard Labaudiniere, a chemist at a Glaxo research facility near Paris, France. (App. at 58a, ¶53). Fifteen days later, Glaxo's PDE V team tested, for the first time, compounds that embodied the skeleton of the Vanderbilt compound, including GR30040X:



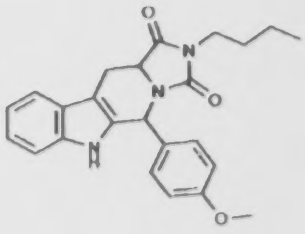
GR 30040X

(App. at 58a-59a, ¶¶54-56).

Dr. Labaudiniere directed one of the Glaxo chemists under his supervision, Dr. Alain Daugan, to make modifications to GR 30040X to improve its potency as a PDE V inhibitor. (App. at 60a, ¶57). The undisputed evidence at trial showed that the very first thing that Dr. Daugan did to modify GR30040X was to simultaneously replace of the pyridine ring with a combination of a phenyl ring **and** an electron-donating methoxy substituent: , which resulted in the synthesis of GF173321X on September 23, 1992, shown here along side 8 – 4 hydroxy phenylthio-IBMX:



8-(4-Hydroxy phenylthio)-IBMX



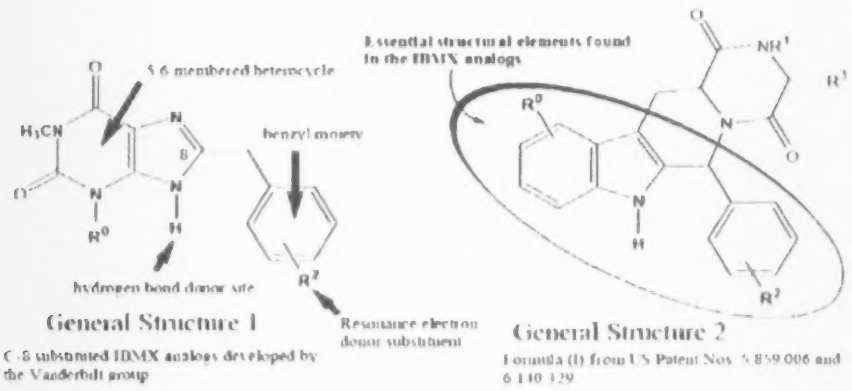
GF 173321X

(App. at 74a-75a, ¶¶79-80). As they did in the case of the Vanderbilt 8-(4-hydroxy phenylthio)-IBMX compound, these changes dramatically improved the

GR30040X's potency in inhibiting PDE5. Less than two months later, Dr. Daugan made modifications to the upper right portion of the compound, resulting in the synthesis of the first of the compounds claimed in the patents. (App. at 75a, ¶81).

Following its application for the Patents, Glaxo assigned its rights in them to Respondent ICOS Corporation ("ICOS"). (App. at 33a-34a, ¶3). It was undisputed at trial that the compounds claimed in the patents incorporated the structural elements reflected in the PDE V inhibitor developed by Vanderbilt and communicated to Glaxo:

FIGURE 1

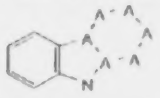
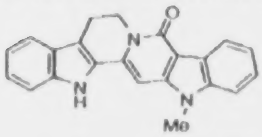


(App. at 72a, ¶76; 81a, ¶90). The sole named inventor on the patent applications and the Patents is Dr. Daugan. (App. at 36a, ¶9)

Lower Court Proceedings. Vanderbilt filed a complaint requesting that the Court issue and order, pursuant to 35 U.S.C. §256, directing the Director of Patents at the United States Patent and Trademark

Office ("PTO") to correct the certificates of the two Patents by adding Drs. Corbin, Francis and Konjeti as joint inventors of the compounds along with Dr. Daugan. (App. at 32a). In its pretrial statement, at trial before the District Court, and in its post trial briefs Vanderbilt asserted that the burden of proof to be applied to Vanderbilt's claim under 35 U.S.C. § 256 should be a preponderance of evidence. (39a n. 8). Vanderbilt further asserted that, even under a more onerous clear and convincing burden, the evidence demonstrated that the Vanderbilt scientists had made a significant contribution to the invention of the claimed compounds, such that the Patents should be corrected to add the Vanderbilt scientists as joint inventors with Dr. Daugan.

As the likely means by which the information supplied by the Vanderbilt scientists to Glaxo could have contributed to the discovery of the claimed compounds, Vanderbilt demonstrated that a search on Glaxo's computerized compound database in April 1992 using the basic structure of Vanderbilt's 8-(4-hydroxy phenylthio)-IBMX compound would have led to the identification of the GR30040X compound that also contained that structure. (App. at 72a-74a, ¶¶76-78). Vanderbilt also proved that the story of the identification of GR30040X that Dr. Daugan, Glaxo and ICOS had been telling to the scientific community and to the District Court from the 1990's through the beginning of the trial was false. (App. at 61a-63a, ¶¶60-64; 70a, ¶¶71-72). At trial ICOS proffered a new story suggesting that GR30040X had been identified

through a search of the database using the carboline structure  contained another compound, GR35273X  (App. at 64a, ¶65). Vanderbilt countered with evidence, including minutes of meetings of the Glaxo PDE V team, which showed that the Glaxo scientists did not consider the carboline structure to be a significant component of GR35273X until at least October 1992, many months after GR30040X had been identified and a month after Dr. Daugan made the modifications, consistent with the Vanderbilt compound, to create GF173321X. A key piece of the evidence introduced by Vanderbilt was an English translation of minutes from an October 1992 meeting of the Glaxo scientists. (App. at 66a, n. 40).

The District Court, following precedent from the Court of Appeals, applied a clear and convincing evidence standard in evaluating the evidence. (App. at 38a-39a). The District Court erroneously failed to consider the English translation of the October 1992 meeting minutes that had been admitted into evidence (App. at 66a, n. 40) and, without considering the fact that Glaxo and ICOS' original story was proven false, concluded that it was equally plausible that GR30040X was identified through a search of the Glaxo database using either the 8-(4-hydroxy phenylthio)-IBMX compound provided by Vanderbilt to Glaxo or the GR35273X compound. (App. at 81a-82a, ¶91).

Notwithstanding the District Court's error with respect to the October 1992 minutes, and the District Court's consideration of the evidence against a clear and convincing burden, the District Court found that Vanderbilt's scientists contributed to the process through which Dr. Daugan invented the compounds claimed in the Patents. (App. at 80a, ¶87). The District Court also found that Glaxo made use of Vanderbilt's "disclosure that 8-(4-OH-PT)-IBMX was "160-fold more potent that the parent IMBX and 6-fold more potent than the best existing inhibitor, zaprinast." (App. at 80a, ¶88). "There was consensus among the witnesses at trial that the 160-fold result would have commanded attention." (App. at 81a, ¶89).

> Defendant's position [that Glaxo made no use of Vanderbilt's disclosures] is also untenable in view of the fact that, although they are (in whole) different molecules having different properties, 8-(4-OH-PT)-IMBX, GR30040x, GF173321x, and the claimed compounds share a common scaffold having a common shape (three-dimensional configuration). It is the court's understanding that the shape of an inhibitor is directly related to its ability to bind to the enzyme. Corbin communicated to Glaxo on several occasions the importance of the spacial relationships of the substituents he was investigating: for example, Corbin's April 1991 minuscript, discussing the 8-position substituent (*supra* no. 29), and the 1992 Research Proposal, discussing the affinity of the 1, 2 and 8-position modifications (*supra* nos. 51, 77).

> Further, there is a close proximity in time of the relevant events which renders plausible plaintiff's theory that Glaxo did take note of 8-(4-OH-PT)-IMBX and incorporated the "Vanderbilt Structural Features" into the beta-carboline research it was conducting.FN51

(App. at 81a, ¶¶90, 91). Nonetheless, "compelled by Federal Circuit precedent," the District Court found that the Vanderbilt scientists' contributions were not sufficient to qualify them as joint inventors of the patented compounds. (App. at 80a, ¶88).

The precedent which compelled the District Court to conclude that the Vanderbilt scientists did not jointly invent the claimed compounds was the Court of Appeal's opinion in *American Bioscience*.

> Indeed, on facts analogous to those at bar,[FN49] the Federal Circuit in *The Board of Education of the Board of Trustees of Florida State University v. American Bioscience, Inc.*, 333 F.3d 1330 (Fed. Cir. 2003) (hereinafter, "*American Bioscience*"), declined to add as inventors scientists who contributed the "starting materials" for a chemical compound. The Court there held that conception of a chemical compound requires "a conception of the specific compounds being claimed, with all of their component substituents." *Id.* at 1340. To put the point another way, "[h]aving in mind specific portions of a claimed compound is not the same as conceiving the compound with all of its components." *Id.*

(App. at 78a-79a, ¶84). As a result of some less than clear statements in that opinion, the District Court read *American Bioscience* as establishing a rule that, in order to be a joint inventor of a chemical compound a person must conceive of the claimed compound in its entirety.

> Because there is no evidence that Corbin, Francis and Konjeti ever conceived the "specific chemical structure of the compound" claimed, *Burroughs Wellcome*, 40 F.3d at 1230, or "the compound with all of its components," *American Bioscience*, 333 F.3d at 1340, or communicated that compound to Glaxo,[FN50] plaintiff has failed to demonstrate, by clear and convincing evidence, that Corbin, Francis and Konjeti are coinventors of the patents at issue.

(App. at 79a-80a, ¶86). Under the bright line rule that the District Court divined from *American Bioscience*, any contribution to the invention of a chemical compound that did not rise to the level of conceiving the entire compound is, by definition, "prosaic" and not enough to merit joint inventor status. (App. at 80a, ¶87).

Vanderbilt appealed the District Court's decision to the Court of Appeals, and asserted that the District Court had committed error by (1) imposing a clear and convincing burden of proof rather than a preponderance of evidence standard; (2) failing to consider key evidence such as the October 1992 minutes; and (3) applying an incorrect standard for determining joint inventor status. The Court of

Appeals panel was unanimous in finding that the bright line rule that the District Court applied was not consistent with 35 U.S.C. Section 116, which sets no explicit lower limit on the quantum or quality of inventive contribution required for a person to qualify as a joint inventor. (App. at 19a, 22a-23a, 25a). However, instead of remanding the case to the District Court with directions that it review the evidence in light of the proper standard, the majority of the Court of Appeals panel, over the remaining judge's dissent, proceeded to apply the correct standard to some of the factual findings stated in the District Court's opinion and, without comment on the District Court's failure to consider the October 1992 minutes, concluded that the Vanderbilt failed to meet a clear and convincing evidence burden with respect to that standard. (App. at 23a).

As for Vanderbilt's assertion regarding the proper burden of proof, the Court of Appeals remarked:

> We express no view on whether Vanderbilt would prevail under a preponderance of the evidence test. Vanderbilt is of course free to seek *en banc* reconsideration of our settled law on this issue.

(App. at 17a-18a, n. 3).

Vanderbilt filed a petition with the Court of Appeals seeking panel rehearing and rehearing *en banc*, both of which were denied by the Court of Appeals. (App. at 86a).

REASONS FOR GRANTING THE PETITION

Neither the language of 35 U.S.C. §256 nor its legislative history indicate that Congress intended that the burden of proof in an action to correct the inventors named on a patent be higher than the preponderance of evidence standard normally imposed upon civil actions. Notwithstanding that fact, and for reasons that do not withstand even scant scrutiny, the Court of Appeals has improperly imposed a clear and convincing evidence standard upon parties, such as Vanderbilt, who bring civil actions under the statute. In addition, having found that the District Court measured the evidence against an incorrect legal standard for determining joint inventorship, the Court of Appeal's decision not to remand Vanderbilt's claim to the District Court for reconsideration of the evidence in light of the proper legal standard is in direct contradiction of the controlling precedent of this Court's decision in *Pullman-Standard v. Swint*, 456 U.S. 273 (1982). For either or both of these reasons, Vanderbilt's petition should be granted.

I. THE COURT OF APPEALS SHOULD NOT IMPOSE A CLEAR AND CONVINCING EVIDENCE BURDEN ON A STATUTORY CIVIL ACTION WHERE THERE IS NO INDICATION IN THE STATUTE OR ITS LEGISLATIVE HISTORY THAT CONGRESS INTENDED A BURDEN OF PROOF HIGHER THAN THE PREPONDERANCE OF EVIDENCE STANDARD NORMALLY IMPOSED UPON CIVIL ACTIONS.

35 U.S.C. §256 permits the correction of a patent certificate so that it accurately reflects the identity of the inventor or joint inventors. There is no language in Section 256 to suggest that Congress intended that the burden of proof imposed upon parties seeking to correct the named inventors on a patent should not be the normal preponderance of evidence standard that is customarily applied to civil actions. Section 256 simply states that "[t]he court before which such matter is called in question may order correction of the patent on notice and hearing of all parties concerned and the Director shall issue a certificate accordingly." 35 U.S.C. §256. Likewise, there is nothing in the legislative history of the statute that suggests that Congress intended that the burden of proof be higher than a preponderance of evidence. When Congress has intended a higher burden, it has very capably indicated such intent. *See e.g.*, 35 U.S.C. §273(b)(4).[1]

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[1] 35 U.S.C. §273 provides a defense to liability for infringement of a method patent where the defendant can show that it had been using the method for at least one year prior to the filing of the patent. §273(b)(4) provides:

While there is no single rule of statutory interpretation that guides a court in ascertaining the appropriate proof burden imposed on a statutory civil action when both a statue and its legislative history are silent, *Alaska Dept. of Environmental Conservation v. EPA*, 540 U.S. 461, 494 n. 17 (2004), the default presumption in civil litigation is that the movant bears the burden under a preponderance of the evidence standard. *Harman & MacLean v. Huddleston*, 459 U.S. 375, 390 (1983); *Addington v. Texas*, 441 U.S. 418, 423 (1979).

The Federal Circuit, which has exclusive appellate jurisdiction at the Court of Appeals level over claims under 35 U.S.C. §256, has departed from the default rule and requires parties seeking to correct a patent under that statute to prove that a correction is necessary by clear and convincing evidence. *Hess v. Advanced Cardiovascular Sys., Inc.*, 106 F.3d 976 (Fed. Cir. 1997), *Eli Lilly v. Aradigm Corp.*, 376 F.3d 1352 (Fed. Cir. 2004)[2]. The stated basis that the Court of Appeals' departure can be summarized as follows: (1) pursuant to 35 U.S.C. §282, an patent issued by the PTO is presumed valid; (2) because a patent is presumed valid, the inventors named on the patent should be presumed correct; and (3) there is a risk that

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> **Burden of proof.**---A person asserting the defense under this section shall have the burden of establishing the defense by clear and convincing evidence.

35 U.S.C. §273(b)(4).

[2] As Judge Lourie's dissent in *Eli Lilly* reveals, the Court of Appeals is not unanimous in its belief that it is logical to impose a clear and convincing burden in cases under 35 U.S.C. §256. 376 F.3d at 1370.

parties seeking to correct the inventors named on a patent will "reconstruct" facts relating to their contribution to the conception of the claimed invention. *See Hess v. Adv. Cardio. Sys., Inc.*, 106 F.3d 976, 980 (Fed. Cir. 1997). Such logic fails to justify a heightened burden because (1) a Section 256 claim does not challenge the validity of a patent; (2) there is no factual basis for a presumption, in the context of a Section 256 claim, that the inventors have been correctly identified in a patent; and (3) there is no inherently greater risk of factual reconstruction in the context of a Section 256 claim than in any other civil action.

35 U.S.C. §282 states that a patent, having undergone examination and survived the prosecution process, "shall be presumed valid." That statute goes on to state that invalidity of a patent is a defense to a claim of infringement. Although Section 282 does not express a Congressional intention that a defense of invalidity be held to a heightened burden of proof, because of the presumption of validity, the Court of Appeals has held that, an alleged infringer asserting such a defense must prove invalidity through clear and convincing evidence. *Z4 Technologies, Inc. v. Microsoft Corp.*, 507 F.3d 1340, 1352 (Fed. Cir. 2007).[3] Thus, where an alleged infringer has asserted that a patent is invalid under Section 282(2) because the plaintiff's

[3] The application of the heightened clear and convincing evidence burden to invalidity defenses under 35 U.S.C. §282 has faced increased criticism by commentators arguing that preponderance of evidence is the more appropriate standard in that context. *See generally* Kristen Dietly, Note, *Lightening the Load: Whether the Burden of Proof for Overcoming a Patent's Presumption of Validity Should Be Lowered*, 78 FORDHAM L. REV. 2615 (2010).

applicant "did not himself invent the subject matter sought to be patented" as required for patentability under 35 U.S.C. §102(f), the Court of Appeals has ruled that the infringer was required to prove that assertion though clear and convincing evidence. *BJ Services Co. v. Halliburton Energy Services, Inc.*, 338 F.3d 1368, 1373 (Fed. Cir. 2003)

In contrast, an action under Section 256 cannot be used to invalidate a patent. Section 256 is a "savings provision" and provides only for remedial relief that would protect a patent's validity. *Pannu v. Iolab Corp.*, 155 F.3d 1344, 1350 (Fed. Cir. 1998). Section 256 can be invoked to correct a patent even where an alleged infringer has proven, by clear and convincing evidence, that the patent does not accurately identify the inventors. *Id.*, at 1350. Thus, the presumption of a patent's validity is irrelevant in the context of a Section 256 claim.[4]

There is no factual basis for a presumption that, simply because a patent has been issued, the inventors thereon have been correctly identified. While patent examiners consider whether an applicant's patent claims are obvious based upon, or anticipated by, prior art, it is well known, and the parties in this case stipulated, that the PTO typically undertakes no action to verify that inventors have been correctly

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[4] *Amax Fly Ash Corp. v. United States*, 514 F.2d 541 (Ct. Cl. 1975), upon which the Court of Appeals relied in adopting the clear and convincing evidence burden for Section 256 claims in *Hess*, involved an effort to raise non-joinder of inventors as a basis for invalidating the plaintiff's patent, and not an action under Section 256.

identified and did not undertake any such action in connection with the Patents in this case.

According to the Court of Appeals "the temptation for even honest witnesses to reconstruct, in a manner favorable to their own position, what their state of mind may have been years earlier, is simply too great to permit a lower standard" in Section 256 cases than the clear and convincing standard. *Hess*, 106 F.3d at 980. *See also Amax Fly Ash*, 514 F.2d at 1050 (claim of co-inventorship is viewed with skepticism). However, all parties in litigation want to win, and while there can be significant monetary and other ramifications related to the outcome of a Section 256 claim, they are not necessarily more significant than those related to the outcomes of other types of patent claims to which the preponderance of evidence standard is applied. Indeed, there is no logical basis to conclude that witnesses on either side of a Section 256 claim would be more or less tempted to reconstruct past events in a manner favorable to his or her own position than a witness, for example, in a patent infringement case. Thus, there is no rational justification for applying the higher clear and convincing standard to a co-inventorship claim under Section 256, while the assertion of the same facts in a priority action is subject to the preponderance of evidence standard. *See Eli Lilly*, 376 F.3d at 1370.

Moreover, any concern regarding the dependability of testimony regarding past state of mind (which might exist with respect to any type of civil action) is uniquely and adequately addressed in the inventorship context by the requirement that testimony of invention

be corroborated. *Chen v. Bouchard*, 347 F.3d 1299, 1309 (Fed. Cir. 2003) (purpose of corroboration requirement is to prevent fraud, by providing independent confirmation of the inventor's testimony); *Medichem, S.A. v. Rolabo, S.L.*, 437 F.3d 1157, 1170 (Fed. Cir. 2006)(credibility concerns undergird the corroboration requirement, the purpose of which is to prevent fraud by providing additional safeguard against deception by inventors who may be tempted to mischaracterize past events through testimony). *See also Fina Oil and Chemical Co. v. Ewen*, 123 F.3d 1466, 1474 (Fed. Cir. 1997).[5]

In short, the standard burden of proof in civil litigation should be applied to claims under Section 256. As the Supreme Court observed in *Addington v. Texas*, 441 U.S. 418, 423-25 (1979), in the typical civil case involving private parties and monetary disputes in which society has minimal concern, the plaintiff's burden is preponderance of evidence. The higher clear and convincing evidence burden is reserved for "civil cases involving allegations of fraud or some other quasi-criminal wrongdoing by the defendant."

> The interests at stake in those cases are deemed to be more substantial than mere loss of money and some jurisdictions accordingly reduce the risk to the defendant of having his reputation tarnished erroneously by increasing the plaintiff's burden of proof. Similarly, this Court

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[5] The fact that the Vanderbilt scientists' testimony regarding their discovery of the novel PDE5 inhibitor structure reflected in 8-(4-OH-PT)-IBMX was fully corroborated by contemporaneous documents has never been disputed.

> has used the "clear, unequivocal and convincing" standard of proof to protect particularly important individual interests in various civil cases. *See, e.g., Woodby v. INS*, supra, at 285 [87 S.Ct. at 487] (deportation); *Chaunt v. United States*, 364 U.S. 350, 353 [81 S.Ct. 147, 149, 5 L.Ed.2d 120] (1960)(denaturalization); *Schneiderman v. United States*, 320 U.S. 118, 125, 159 [63 S.Ct. 1333, 1336, 1353, 87 L.Ed. 1796] (1943)(denaturalization).

Id. at 423-25. As the Supreme Court has more recently observed, under the Patent Act a patent is personal property, and there is no presumption that the rights attendant thereto cannot be quantified in terms of money. *eBay, Inc. v. Mercexchange, LLC*, 547 U.S. 388 (2006); 35 U.S.C. §261. Thus, whatever interests may be implicated by a claim under Section 256, they are not the type of "important individual interests" that warrant the imposition of a burden of proof beyond preponderance of evidence.

For these reasons, Vanderbilt submits that the burden of proof applied to civil actions under 35 U.S.C. §256 should be preponderance of evidence and the Court of Appeals decisions imposing a higher clear and convincing evidence burden of proof, which the District Court followed, were in error. It is well settled that the application of the wrong burden of proof cannot be harmless error. *See Putnam Resources v. Pateman*, 958 F.2d 448, 471 (1st Cir. 1992)(district court's use of improper burden of proof cannot be considered harmless); *Chen v. General Accounting Office*, 821 F.2d

732, 741 n. 13 (D.C. Cir. 1987)(same); *Price v. Symsek*, 988 F.2d 1187, 1194 (Fed. Cir. 1993)(same). *See also SSIH Equipment S.A. v. U.S. Int'l Trade Comm'n*, 718 F.2d 365, 383 (Fed. Cir. 1983)("the degree of proof below affects the appellate decision whether to affirm or reverse . . . .").

This Court should not sanction a lower court's legislation of a heightened burden of proof into a statutory cause of action when there is no indication in the statute or its legislative history that Congress intended a burden beyond preponderance of evidence and there is no logical basis for a heightened burden. Vanderbilt's petition, therefore, should be granted.

II. THE DECISION OF THE COURT OF APPEALS NOT TO REMAND THE CASE CONTRADICTS THIS COURT'S DECISION IN *PULLMAN-STANDARD V. SWINT*.

The Decision of the Court of Appeals is in direct conflict with *Pullman-Standard v. Swint*, 456 U.S. 273 (1982). Where, as in this case, the District Court has committed error in the interpretation and application of the patent statute, and its factual findings "rest on an erroneous view of the law," those factual findings may be set aside on that basis, regardless of whether they are otherwise clearly erroneous. *Pullman-Standard*, 456 U.S. at 287; *W.L. Gore v. Garlock*, 721 F.2d 1540, 1547 (Fed. Cir. 1983).

As the Supreme Court has noted, "[w]hen an appellate court discerns that a district court has failed to make a finding because of an erroneous view of the

law, the usual rule is that there should be a remand for further proceedings to permit the trial court to make the missing findings," and "where findings are infirm because of an erroneous view of the law, a remand is the proper course unless the record permits only one resolution of the factual issue." *Pullman-Standard*, 456 U.S. at 291-92. *See also W.L. Gore*, 721 F.2d at 1547 (where district court's finding rests upon erroneous view of law, appellate court should not "engage in what would be an inappropriate reweighing of facts"); *Impax Labs., Inc. v. Aventis Pharm., Inc.*, 468 F.3d 1366, 1383 (Fed. Cir. 2006); *Trovan, Ltd. v. Sokymat SA*, 299 F.3d 1292, 1310 (Fed. Cir. 2002)(where district court did not properly construe patent claims remand was required for resolution of factual issues regarding whether alleged infringer was a co-inventor); *United States v. Hasan*, 609 F.3d 1121, 1129 (10th Cir. 2010)(when the court of appeals notices a legal error, it is not ordinarily entitled to weigh the facts itself and reach a new conclusion; instead, it must remand to the district court for it to make a new determination under the correct law).

The Court of Appeals decision is in direct conflict with this Court's opinion in *Pullman*. Here the record clearly permits more than one resolution of the relevant factual issues. As Judge Dyk noted in his concurring and dissenting opinion:

> While the district court found that the Vanderbilt scientists made some contribution, it has not told us exactly what that contribution was or why that contribution was not enough to make the Vanderbilt scientists joint inventors

> under the correct standard. If the Vanderbilt scientists made contributions, as the district court found, the fact that those contributions may not have been "appropriated by Dr. Labaudiniere for his substructure search," Majority Op. at 15 (App. at 18a) does not foreclose the possibility that the Vanderbilt scientists' contribution was sufficient to make them joint inventors.
>
> Because the district court's findings were either contradictory or tainted by legal error, I think we must vacate the judgment and remand in order that the court may make factual findings under the proper law.

(App. at 30a). Rather than attempt to reach its own factual findings or to discern how the District Court would have viewed the facts had it applied the appropriate standard, the Court of Appeals should have remanded the case to the District Court with instructions that it reconsider all of the evidence in light of the appropriate standard. *Pullman* requires that the Court of Appeals' decision be overturned and that this case be remanded to the District Court for factual findings that are not "tainted by legal error."

This Court should not sanction an appellate court's usurpation of a trial court's role in weighing evidence against the appropriate legal standard for the claims in suit. Vanderbilt's petition, therefore, should be granted.

CONCLUSION

For all of the forgoing reasons, the petition for a writ of certiorari should be granted.

Respectfully submitted this 21st day of September, 2010,

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APPENDIX

APPENDIX

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APPENDIX A

UNITED STATES COURT OF APPEALS FOR THE FEDERAL CIRCUIT

*Revised April 9, 2010

No. 2009-1258

[Filed April 7, 2010]

VANDERBILT UNIVERSITY,

Plaintiff-Appellant,

v.

ICOS CORPORATION,

Defendant-Appellee.

Robert S. Brennen, Miles & Stockbridge P.C., of Baltimore, Maryland, argued for plaintiff-appellant. With him on the brief were Donald E. English, Jr.; Kurt C. Rommel and James T. Carmichael, of McLean, Virginia. Of counsel were Leona Marx and David Williams, II, Vanderbilt University, of Nashville, Tennessee.

* Revised to correct name of attorney Robert S. Brennen.

Kevin M. Flowers, Marshall, Gerstein & Borun LLP, of Chicago, Illinois, argued for defendant-appellee. With him on the brief were Thomas I. Ross and Matthew C. Nielsen. Of counsel on the brief were Paul R. Cantrell, Donald L. Corneglio and Dan L. Wood, Eli Lilly and Company, of Indianapolis, Indiana.

Appeal from the United States District Court for the District of Delaware in case no. 05-CV-506, Judge Sue L. Robinson.

Before MICHEL, Chief Judge, CLEVENGER and DYK, Circuit Judges.

Opinion for the court filed by Circuit Judge CLEVENGER. Opinion concurring in part and dissenting in part filed by Circuit Judge DYK.

CLEVENGER, Circuit Judge.

This is an appeal from the United States District Court for the District of Delaware in a patent action that Vanderbilt University ("Vanderbilt") brought against ICOS Corporation ("ICOS") on July 20, 2005. Vanderbilt filed suit under 35 U.S.C. § 256 alleging that Vanderbilt scientists Jackie D. Corbin ("Dr. Corbin"), Sharron H. Francis ("Dr. Francis"), and Sekhar R. Konjeti ("Dr. Konjeti") (collectively the "Vanderbilt Scientists") should be added as joint inventors on U.S. Patent Nos. 5,859,006 ("the '006 patent") and 6,140,329 ("the '329 patent"). The district court rendered its findings of fact and conclusions of law in a January 27, 2009 opinion. Vanderbilt Univ. v. ICOS Corp., 594 F. Supp. 2d 482 (D. Del. 2009). The district court entered final judgment on January 29,

2009, concluding that Vanderbilt failed to prove that the Vanderbilt Scientists are joint inventors of the '006 and '329 patents. Vanderbilt appeals the district court's final judgment. For the reasons stated below, we affirm.

I

This case involves compounds and methods for treating erectile dysfunction, including the compound known as tadalafil, a PDE5 inhibitor and the active ingredient in the drug Cialis®. PDE5 is a phosphodiesterase enzyme found in smooth muscle cells that binds to and hydrolyzes or breaks down cGMP, a cyclic nucleotide found in smooth muscle tissues. In normal function, cGMP binds with and activates a cGMP-dependent protein kinase which results in relaxation and dilation of the smooth muscle cell. PDE5 inhibitors bind to PDE5 and prevent it from binding with and breaking down cGMP.

Drs. Corbin and Francis are employed by Vanderbilt University and were among the first to discover PDE5 in the late 1970s. Since that time, Drs. Corbin and Francis have worked on both the development of cGMP analogs and PDE5 related research.

In December 1988, Dr. Corbin submitted a research proposal to Glaxo Inc. ("Glaxo")[1] requesting it sponsor

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[1] Glaxo Inc., later renamed Glaxo Wellcome Inc., was a North Carolina corporation that merged with SmithKline Beecham to form Glaxo SmithKline in 2001. Glaxo Group Limited ("Glaxo U.K.") was a U.K.-based subsidiary of Glaxo. At all times relevant to this litigation, Glaxo maintained a research facility in Les Ulis,

his research to develop cGMP analogs. The proposal listed new cGMP analogs that Dr. Corbin hoped would activate cGMP-dependent protein kinase.

In June 1989, Glaxo entered into an agreement with Dr. Corbin through Glaxo's "Cardiovascular Discovery Grant" program to underwrite the Vanderbilt Scientists' research of cGMP analogs. Under the agreement, the University retained ownership of intellectual property, but Glaxo was granted a license agreement to any discoveries. During the three years of the program, Drs. Corbin, Francis, and Konjeti submitted numerous presentations and progress reports to Glaxo.

In November 1990, Dr. Corbin sent an abstract to Glaxo U.K. disclosing his discovery that the potency of cGMP analogs is enhanced by adding a phenyl ring at the 8-position. Meanwhile, the Vanderbilt Scientists continued to work on improving potency with new cGMP analogs. In May 1991, however, Glaxo indicated to Dr. Corbin its concern that cGMP analogs do not work well as orally-administered drugs and encouraged the Vanderbilt Scientists to shift their future focus to PDE5 inhibitors.

Outside of the Glaxo program, the Vanderbilt Scientists continued to work on other research interests. In November 1991, the Vanderbilt Scientists applied the results of their cGMP analog research to synthesize a new PDE5 inhibitor. The Vanderbilt Scientists used a 3-isobutyl-1-methylxanthine

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France ("Glaxo France"). The patents in suit list a Glaxo France scientist as the sole inventor and are assigned to ICOS.

("IBMX") compound because it was a cheap and readily available PDE5 inhibitor that is easily substituted at the 8-position. Building upon their earlier research, the Vanderbilt Scientists attached a phenyl ring to the 8-position of the compound and attached an electron-donating hydroxyl group at the 4 position of the phenyl ring. By applying the results of their cGMP research to IBMX, the Vanderbilt Scientists created a PDE5 inhibitor they thought was 160 times more potent in inhibiting PDE5 than the original IBMX molecule. Dr. Corbin drafted a letter to Vanderbilt's general counsel disclosing possible therapeutic uses for the new IBMX analogs, including the treatment of male impotence.

In December 1991, during discussions regarding a new research agreement, Dr. Corbin mentioned Vanderbilt's work on PDE5 inhibitors to Dr. Barry Ross, a scientist at Glaxo U.K. On January 3, 1992, Dr. Corbin sent a research proposal to Glaxo U.K. detailing the test results of the cGMP analogs developed under the first research agreement. In the proposal, Dr. Corbin also described the Vanderbilt Scientists' IBMX analog that was 160-fold more potent as a PDE5 inhibitor than the original IBMX molecule. Dr. Corbin explained the Vanderbilt Scientists' overall strategy that "the potencies of existing inhibitors . . . could be enhanced by appending groups that would allow the inhibitors to more closely resemble the entire cyclic GMP molecule." Dr. Corbin proposed that Glaxo fund the Vanderbilt Scientists' work on PDE5 inhibitors going forward. Dr. Corbin also noted in the January letter that "the cG kinase has important disease-related functions other than the induction of vascular smooth muscle relaxation." Male impotence

was listed as an area of interest, though Glaxo was not researching male impotence at the time.

On February 3, 1992, Drs. Corbin and Francis met with Dr. Ross regarding the January proposal. Later that month, on February 24, Dr. Corbin sent a more detailed research proposal to Dr. Ross which disclosed the exact design of the Vanderbilt IBMX analog. The detailed research proposal also identified a table of IBMX and zaprinast[2] analogs that Vanderbilt proposed for further testing. Many of the listed compounds contain what Vanderbilt now refers to as the "Vanderbilt Structural Features" of Vanderbilt's IBMX analog.

On March 11 and 12, 1992, Glaxo France tested 26 compounds for PDE5 inhibition, including a compound it designated GR35273x.

On April 8, 1992, Dr. Ross forwarded copies of Vanderbilt's February 24, 1992 proposal to six Glaxo scientists, including Dr. Richard Labaudiniere, the head of chemistry and leader of the PDE5 project at Glaxo France.

On April 23, 1992, Glaxo France tested 29 compounds for PDE5 inhibition, including a beta-carboline compound designated GR30040x. Vanderbilt claims all of the tested compounds make some use of the Vanderbilt Structural Features with 11 of the 29 compounds containing nearly all of the Vanderbilt Structural Features. Based on the PDE5

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[2] Zaprinast was the most powerful known PDE5 inhibitor at the time of the research proposal.

inhibition test results, Dr. Labaudiniere identified GR30040x as a lead compound for further research on PDE5 inhibition. Dr. Labaudiniere assigned the further GR30040x research to Dr. Alain Claude-Marie Daugan, the named inventor on the patents at issue, as a separate study. In the course of testing various modifications to the GR30040x compound between June 1992 and January 1994, Dr. Daugan discovered tadalafil, the claimed compound at issue in this case.

II

In 1991, Glaxo assigned to ICOS the rights, title, and interest in the compounds covered by the patents at issue. Vanderbilt brought this suit under 35 U.S.C. § 256 against ICOS to correct inventorship of the '006 and '329 patents. Vanderbilt asserts that the Vanderbilt Scientists should be added as joint inventors. According to Vanderbilt, the GR30040x compound could not have been identified by Dr. Labaudiniere as the lead compound without his use of the Vanderbilt Structural Features. Nor could tadalafil have been identified by Dr. Daugan without his reliance on Vanderbilt's work. The district court held a bench trial and found in favor of ICOS.

In its analysis, the district court noted that 35 U.S.C. § 116, the applicable section for joint inventorship, sets "no explicit lower limit on the quantum or quality of inventive contribution required for a person to qualify as a joint inventor." Vanderbilt Univ. v. ICOS Corp., 594 F. Supp. 2d 482, 504 (D. Del. 2009) (quoting Fina Oil & Chem. Co. v. Ewen, 123 F.3d 1466, 1473 (Fed. Cir. 1997)). The district court further noted that "a person is a joint inventor 'only if he contributes to the conception of the claimed

invention.'" Id. (quoting Eli Lilly & Co. v. Aradigm Corp., 376 F.3d 1352, 1458-59 (Fed. Cir. 2004)). After a summary of the law regarding conception of chemical compounds, the district court concluded that "conception of a chemical substance includes knowledge of both the specific chemical structure of the compound and an operative method of making it" and "does not occur unless one has a mental picture of the structure of the chemical." Id. (quoting Burroughs Wellcome Co. v. Barr Labs., Inc., 40 F.3d 1223, 1230 (Fed. Cir. 1994) and Amgen, Inc. v. Chugai Pharm. Co., Ltd., 927 F.2d 1200, 1206 (Fed. Cir. 1991)). The district court determined that the Vanderbilt Scientists could not be co-inventors because they never "conceived the specific chemical structure of the compound claimed or the compound with all of its components." Id. at 505 (citations omitted).

To guide its analysis, the district court reviewed our decision in American BioScience and concluded the case contained similar facts and thus controlled its decision. Id. at 504-05. The district court recognized that in American BioScience we declined to add inventors who provided the "starting materials" for a chemical compound. See Bd. Of Educ. ex rel. Bd. of Trustees of Fla. State Univ. v. Am. BioScience Inc., 333 F.3d 1330 (Fed. Cir. 2003) ("American BioScience"). The district court found that "[t]he 'Vanderbilt Structural Features' constitute no more than a 'specific portion[] of a claimed compound' in the language of American BioScience." Vanderbilt Univ., 594 F. Supp. 2d at 505.

The district court concluded that "[b]ecause there is no evidence that [the Vanderbilt Scientists] ever conceived the 'specific chemical structure of the

compound' claimed, Burroughs Wellcome, 40 F.3d at 1230, or 'the compound with all of its components,' American BioScience, 333 F.3d at 1340, or communicated that compound to Glaxo, plaintiff has failed to demonstrate by clear and convincing evidence, that Corbin, Francis and Konjeti are coinventors of the patents at issue." Id. The district court noted that "even if the court were to find that plaintiff's disclosure of [the Vanderbilt Structural Features] led to the identification of GR30040x and the subsequent discovery of tadalafil, American BioScience precludes the result plaintiff seeks: namely, that the contribution of a molecular scaffold in the context of one molecule . . . renders the disclosing party or parties inventors of a different family of molecules containing the same scaffold." Id. at 506-07.

Even after reaching the conclusion that its decision was bound by American BioScience, the district court provided a detailed analysis of the remaining facts of the case. First, the court noted that "[t]his is not to say that Corbin, Francis, and Konjeti did not make contributions to Daugan's inventive process; only that, under the applicable law, these contributions fall more into the category of 'prosaic' contributions because they did not conceive the invention as claimed." Id. at 505. After again reviewing the conflicting stories of the parties, the district court alternatively noted that "the court views plaintiff's theory . . . and defendant's story . . . equally plausible with respect to the identification of GR30040x." Id. at 506. Also, in the absence of any evidence of collaboration between the Vanderbilt Scientists and Dr. Daugan, the district court rejected Vanderbilt's claim to have contributed to Dr. Daugan's identification of tadalafil. Id. at 505-06.

III

We begin by reviewing our case law on joint inventorship. The statutory requirements for joint inventorship are found in 35 U.S.C. § 116 which states, in pertinent part:

> When an invention is made by two or more persons jointly, they shall apply for patent jointly and each make the required oath, except as otherwise provided in this title. Inventors may apply for a patent jointly even though (1) they did not physically work together or at the same time, (2) each did not make the same type or amount of contribution, or (3) each did not make a contribution to the subject matter of every claim of the patent.

35 U.S.C. § 116 (1988).

Section 116 was amended, in relevant part, in 1984 to clarify the law of joint inventorship by codifying the principles set forth in Monsanto Co. v. Kamp, 269 F. Supp. 818 (D.D.C. 1967). See Kimberly-Clark Corp. v. Proctor & Gamble Distrib. Co., Inc., 973 F.2d 911, 916 (Fed. Cir. 1992). The court in Monsanto stated:

> A joint invention is the product of collaboration of the inventive endeavors of two or more persons working toward the same end and producing an invention by their aggregate efforts. To constitute a joint invention, it is necessary that each of the inventors work on the same subject matter and make some contribution to the inventive thought and to the final result. Each needs to perform but a part of

> the task if an invention emerges from all of the steps taken together. It is not necessary that the entire invention concept should occur to each of the joint inventors, or that the two should physically work on the project together. One may take a step at one time, the other an approach at different times.

Monsanto, 269 F. Supp. at 824.

In Kimberly-Clark, we applied section 116 to a situation where Proctor & Gamble wished to attribute inventor status to one of its employees who did not collaborate with the named inventor. 973 F.2d at 912-13. While both employees worked on the same subject matter, the court noted that the named inventor "worked alone and was completely unaware of earlier work done by other [] employees." Id. at 913. The court reviewed the amendments and Monsanto and stated that:

> For persons to be joint inventors under Section 116, there must be some element of joint behavior, such as collaboration or working under common direction, one inventor seeing a relevant report and building upon it or hearing another's suggestions at a meeting. Here there was nothing of that nature. Individuals cannot be joint inventors if they are completely ignorant of what each other has done until years after their individual efforts. They cannot be totally independent of each other and be joint inventors.

Kimberly-Clark, 973 F.2d at 917.

A primary focus of section 116 has thus always been on collaboration and joint behavior. A person must contribute to the conception of the claimed invention to qualify as a joint inventor. Eli Lilly & Co. v. Aradigm Corp., 376 F.3d 1352, 1359 (Fed. Cir. 2004). Yet, each contributor need not have their own contemporaneous picture of the final claimed invention in order to qualify as joint inventors. See Fina Oil & Chem. Co. v. Ewen, 123 F.3d 1466, 1473 (Fed. Cir. 1997) ("One need not alone conceive of the entire invention, for this would obviate the concept of joint invention."). Rather, "the qualitative contribution of each collaborator is the key – each inventor must contribute to the joint arrival at a definite and permanent idea of the invention as it will be used in practice." Burroughs Wellcome Co. v. Barr Labs. Inc., 40 F.3d 1223, 1229 (Fed. Cir. 1994). The interplay between conception and collaboration requires that each co-inventor engage with the other co-inventors to contribute to a joint conception.

Inventorship is a question of law that we review without deference. Ethicon, Inc. v. U.S. Surgical Corp., 135 F.3d 1456, 1460 (Fed. Cir. 1998). We review the underlying findings of fact for clear error. See Hess v. Advanced Cardiovascular Sys., Inc., 106 F.3d 976, 980 (Fed. Cir. 1997).

IV

Vanderbilt raises two arguments on appeal. First, Vanderbilt argues that its disclosure of the Vanderbilt Structural Features led to Glaxo France's identification of the GR30040x molecule incorporating the same molecular scaffold. In this regard, the gist of Vanderbilt's case is that Dr. Labaudiniere could only

have identified GR30040x by using the Vanderbilt Structural Features. Second, Vanderbilt alleges that the key modification to GR30040x that yielded tadalafil was the addition of an electron-donating substituent on the phenyl ring based upon the work of the Vanderbilt Scientists.

There is no dispute raised between the parties regarding the district court's finding that Dr. Labaudiniere at Glaxo France identified GR30040x as a lead compound for research regarding PDE5 inhibition. Thus, as all relevant contact between the Vanderbilt Scientists and Glaxo occurred at Glaxo U.K., Vanderbilt attempts to piece together sufficient facts to demonstrate that the Vanderbilt Structural Features must have been used by Dr. Labaudiniere to identify GR30040x. As Vanderbilt's argument is based largely upon criticizing ICOS's evidence regarding how GR30040x was recognized, we first review Glaxo's version of the story.

ICOS contends that Dr. Labaudiniere independently discovered the compounds to be tested for PDE5 inhibition through his knowledge of beta-carbolines and their vasorelaxation effect. This theory can be found in a paper received by the Journal of Medicinal Chemistry on February 5, 2003, entitled "The Discovery of Tadalafil: A Novel and Highly Selective PDE5 Inhibitor." According to Glaxo, Dr. Labaudiniere became aware of the vasorelaxation effect of beta-carbolines from his review of two references: a 1983 article in the European Journal of Pharmacology ("the Koe article") and a May 1992 article in the Journal of Pharmacology and Experimental Therapeutics ("the Elgoyhen article"). Glaxo claims that Dr. Labaudiniere identified two

beta-carboline compounds, β-CEE and GR35273x, in March 1992 as potential PDE-5 inhibitors. Dr. Labaudiniere then searched an internal database in April 1992 with the beta-carboline core structure of these two molecules and his search yielded GR30040x. Glaxo's internal "PDE V Inhibitors Project Annual Report for the Year Ending 30/4/93" confirms this story.

Vanderbilt takes issue with Glaxo's story because Glaxo's internal testing records indicate that GR30040x was first tested by Glaxo on April 23, 1992. The Elgoyhen article was not published until May 8, 1992. As the district court found, GR30040x could not have been identified based upon the Elgoyhen reference.

At trial, ICOS backed away from the Elgoyhen story and instead argued that Dr. Labaudiniere took GR35273x from another Glaxo program and tested it on March 11 and 12, 1992 for PDE5 inhibition. According to ICOS, Dr. Labaudiniere undertook substructure searches using the tetrahydro beta-carboline scaffold of GR35273x, based upon the "impressive" PDE5 inhibition results and his knowledge from the Koe article, and identified GR30040x, among other compounds. ICOS points to the large number of tetrahydro beta-carbolines tested between March and July 1992 to support its theory.

ICOS also points to Glaxo documents to corroborate various details of its story. For example, the minutes of a Glaxo Cardiovascular Research Management Committee meeting in April 1992 describe GR35273x as a compound used in a different study. In the June 1992 minutes, the same committee noted that

GR35273x displayed a high PDE5 inhibition activity and noted that Glaxo was starting a program testing GR35273x analogs. At the same meeting, GR30040x was identified as a new PDE5 inhibitor.

ICOS also points to testimony of Dr. Labaudiniere and Dr. Daugan to corroborate its theory on the identification of GR30040x. Dr. Labaudiniere testified that he did not have any knowledge about the Vanderbilt Scientists' research until June 1993, he did not consider IBMX as a starting point for his work on PDE5 inhibitors, and he was not aware of anyone at Glaxo France using data relating to IBMX analogs or trying to develop PDE5 inhibitors that would resemble cGMP. Dr. Daugan confirmed his recollection matches that of Dr. Labaudiniere. In sum, ICOS argues that Vanderbilt's case fails for lack of evidence of any joint collaboration on the invention since neither of the Glaxo France scientists had any knowledge of the work of the Vanderbilt Scientists when they did their work relating to the discovery of tadalafil.

Vanderbilt argues a different view of the same facts. First, Vanderbilt points out that GR30040x is never identified in any Glaxo documents as a GR35273x analog. Vanderbilt also argues that a GR35273x substructure search would not yield GR30040x because no documents demonstrate that Glaxo identified the beta-carboline structure in GR35273x as significant until October 1992. Finally, Vanderbilt argues that Glaxo lacks credibility as it had previously claimed GR30040x was identified from a β-CEE search until that was proven false. In sum, Vanderbilt attacks Glaxo's story based upon missing documentary evidence.

Vanderbilt instead proposes that Dr. Labaudiniere reviewed the February 1992 research proposal and conducted a substructure search based upon the Vanderbilt IBMX analog. Vanderbilt points out that in April, just weeks after receiving the February proposal, Glaxo France tested 29 compounds for PDE5 inhibition. Vanderbilt points out a number of structural similarities between the tested compounds and its February research proposal.

Vanderbilt's second argument is that after the GR30040x project was assigned to Dr. Daugan, he added to tadalafil an additional element of the Vanderbilt Structural Features by replacing the pyridine ring in GR30040x with a combination of a phenyl ring and an electron-donating methoxy substituent. Vanderbilt argues that this modification directly uses the results of the Vanderbilt Scientists' research. ICOS responds that the modifications were all part of a standard trial and error procedure that would be tried with any molecules of interest.

The only evidence of record regarding Glaxo's modifications to GR30040x is the testimony of Dr. Daugan and Dr. Labaudieniere. Dr. Daugan testified that "[t]he first thing [he] did in this series was explore the replacement of the pyridinyl[] moiety with other heterocyclic or aromatic moieties." Dr. Labaudiniere testified that there are a standard group of substitutions or additions that would be tried with any molecules of interest. Dr. Labaudiniere characterizes the modifications leading to tadalafil as "obvious" and conducted in a "trial-and-error" fashion. There is no testimony or documentary evidence demonstrating a link between the Vanderbilt Scientists and Dr. Daugan prior to the identification of tadalafil. Indeed,

Vanderbilt admitted in the district court that it had no direct evidence to support its view of the facts; instead Vanderbilt argued that it "need not prove specifically how that occurred, but simply how it logically could have occurred."

V

Vanderbilt's challenge to the stated inventorship of the '006 and '329 patents turns on competing claims to inventorship of GR30040x and to tadalafil. As explained above, Vanderbilt admits that no direct evidence supports its claims to joint inventorship. Nonetheless, Vanderbilt argues that Dr. Labaudiniere could not have identified GR30040x as a lead compound independently; nor could Dr. Daugan have identified tadalafil on his own. ICOS counters Vanderbilt's arguments with direct evidence supporting Dr. Labaudiniere's claim to sole identification of GR30040x and with similar direct evidence pointing to Dr. Daugan's independent discovery of tadalafil.

To succeed on its claim to joint inventorship, Vanderbilt must prevail by clear and convincing evidence. Our precedent has long required proof of misjoinder or nonjoinder of co-inventors by clear and convincing evidence.[3] See Eli Lilly & Co. v. Aradigm

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[3] Vanderbilt recognizes that the clear and convincing evidence test for correction of inventorship is settled law which binds the court. It suggests that the law should be changed to a lower standard of proof, namely preponderance of the evidence, and that under the lower test it should prevail in this case. We express no view on whether Vanderbilt would prevail under a preponderance of the

Corp.,376 F.3d 1352, 1364 (Fed. Cir. 2004); Ethicon v. U.S. Surgical Corp., 135 F.3d 1456, 1460-61 (Fed. Cir. 1998); Hess v. Advanced Cardiovascular Sys., Inc., 106 F.3d 976, 980 (Fed. Cir. 1997). The district court correctly concluded that Vanderbilt failed to meet its burden.

We find no clear error in the district court's factual findings underpinning its determination regarding Glaxo's identification of GR30040x. The district court noted that "there is a close proximity in time of the relevant events which renders plausible plaintiff's theory that Glaxo did take note of [the Vanderbilt IBMX compound] and incorporated the 'Vanderbilt Structural Features' into the beta-carboline research it was conducting." Vanderbilt Univ. v. ICOS Corp., 594 F. Supp. 2d 482, 506 (D. Del. 2009). However, after a thorough review of all of the evidence, the district court concluded "the court views plaintiff's theory (which is devoid of evidence regarding the alleged substructure searches based on [the Vanderbilt IBMX compound]) and defendant's story (which is devoid of the aforementioned foundation) equally plausible with respect to the identification of GR30040x." Id. We agree that Vanderbilt fails to present clear and convincing evidence to support its argument that the work of the Vanderbilt Scientists was appropriated by Dr. Labaudiniere for his substructure search.

As for Vanderbilt's argument that Dr. Daugan made use of the Vanderbilt Scientists' research for the modifications to GR30040x, the district court noted

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evidence test. Vanderbilt is of course free to seek en banc reconsideration of our settled law on this issue.

that "plaintiff admitted that Corbin, Francis and Konjeti never had any direct communication with Daugan regarding this subject matter." Id. at 505 n.50. The district court also noted "a lack of evidence" supporting Vanderbilt's request for an inference that Dr. Labaudiniere communicated the Vanderbilt Structural Features to Dr. Daugan. Id. There is nothing in the record to suggest that these factual findings are erroneous. Thus, Vanderbilt also fails to present clear and convincing evidence to support its argument that the modifications to GR30040x by Dr. Daugan made use of the Vanderbilt Scientists' research.

VI

Vanderbilt makes much of what it perceives to be an error of law committed by the district court. We agree that the district court opinion contains some erroneous statements regarding the law of joint inventorship and a misunderstanding of the relevance of American BioScience to the facts of this case. These errors, however, do not affect the outcome of this appeal and are therefore harmless in context. When tested by the correct law, the facts of the case still require affirmance.

The district court understood our decision in American BioScience to require that each co-inventor have an independent conception of the final compound for a chemical invention. The district court ruled that because the Vanderbilt Structural Features constitute no more than a portion of a claimed compound, the Vanderbilt Scientists cannot, as a matter of law, be joint inventors. Vanderbilt Univ., 594 F. Supp. 2d at 505. The district court hinged this portion of its

opinion on the following language from American Bioscience:

> Having in mind specific portions of a claimed compound is not the same as conceiving the compound with all of its components. One must have a conception of the specific compounds being claimed, with all of their component substituents . . . .

333 F.3d at 1340. Yet, when this language from American BioScience is reviewed in context, the district court's error is clear.

The portion of the opinion quoted by the district court phrased the question under review as "whether the district court erred in determining that the FSU scientists were true inventors of the claimed compounds." Id. (emphasis added). In American BioScience the court was faced with choosing between two competing groups of inventors.

Prior to the invention of the compounds at issue in American BioScience, Dr. Tao, a scientist at Florida State University ("FSU"), left FSU to join a group of scientists at American BioScience that were working on similar subject matter. Id. at 1333-35. Shortly after Dr. Tao joined American BioScience, the company filed a patent application that led to the patent in suit, which claimed three taxol analog compounds. The patent named Dr. Tao and three American BioScience scientists as joint inventors. In the district court, FSU claimed that the patent named the wrong inventors. FSU asserted that three of its scientists, along with Dr. Tao, were the correct team of joint inventors. The district court reviewed the evidence on behalf of both

competing teams of joint inventors, and concluded that the FSU team was the true group of joint inventors. Accordingly, the district court ordered that the three American BioScience scientists be removed from the patent and the patent be corrected to add the three FSU scientists as inventors. Bd. of Educ. v. Am. BioScience, Inc., No. 4:99cv131/RV, 2001 WL 34104924, at *11 (N.D. Fla. 2001).

American BioScience appealed to this court, arguing clear error in the fact findings made by the district court to support its correction of inventorship. Because the record provided no evidence of conception by any of the FSU scientists, acting individually or together, this court found clear error in awarding inventorship to the FSU joint inventor team. Properly understood, American BioScience correctly states the law governing joint inventorship. Absent conception within an inventorship team, there can be no invention.

This court began its inquiry with the statement that "[i]nvention requires conception, and 'conception does not occur unless one has a mental picture of the structure of the chemical . . . or whatever characteristics sufficiently distinguish it. It is not sufficient to define it solely by its principal biological property.'" American BioScience, 333 F.3d at 1340 (quoting Amgen Inc. v. Chugai Pharm. Co., 927 F.2d 1200, 1206 (Fed. Cir. 1991)). This court held that the FSU group could not have been the true inventors unless the group had a complete mental picture of the structure of the chemical compounds at issue, and continued its analysis with the language relied upon by the district court. See id. at 1340 ("One must have a conception of the specific compounds being claimed,

with all of their component substituents, and the record does not support a finding that [anyone in the FSU group] conceived the three claimed compounds . . . .").

While it is true that the court used the term "one" in reference to conception, it is apparent from context that the court was referring to "the inventor" or, in the case of joint inventors, "the group of inventors." Thus, in American BioScience, the court found that the FSU inventors were not part of any group or collaboration that together envisioned the final claimed compounds. This is because "[w]hile Holton may have invented many of the compounds synthesized in his laboratory . . . there is nonetheless no evidence of conception by Holton or anyone else at FSU of analogs having the [required combination of molecules]." Id. at 1341. The court's finding in American BioScience was premised on the fact that the FSU and American BioScience scientists were not working together, but rather competing for the patent rights in the compounds at issue. There was no evidence of conception within the FSU group, and this court found sufficient evidence of conception within the American BioScience group.

Vanderbilt is correct that the district court erred in reading American BioScience to find that each co-inventor must have an independent mental picture of the complete compound claimed. Such an interpretation is clearly wrong under our established precedent. Instead, a group of co-inventors must collaborate and work together to collectively have a definite and permanent idea of the complete invention. Similarly, the district court's statement that "the contribution of a molecular scaffold in the context of one molecule" could never rise to the level of joint

inventorship for "a different family of molecules containing the same scaffold" is in error. Vanderbilt Univ., 594 F. Supp. 2d at 506-07. "The determination of whether a person is a joint inventor is fact specific, and no bright-line standard will suffice in every case." Fina Oil & Chem. Co. v. Ewen, 123 F.3d 1466, 1473 (Fed. Cir. 1997). Our case law was not intended to create such a bright line rule as was used by the district court.

As previously stated, the district court, however, did not rest its opinion solely on this interpretation of our case law. The district court correctly noted that conception requires identification of the specific chemical structure of the compound. The parties agree that Dr. Daugan was the first to conceive of tadalafil. After a careful review of the evidence, the district court concluded that the parties' respective stories about whether the Vanderbilt Scientists contributed to the identification of GR30040x were "equally plausible" and that Vanderbilt failed to produce any evidence of joint invention of tadalafil. For Vanderbilt to succeed in its inventorship claim, it must carry its burden of proof of demonstrating that the Vanderbilt Scientists contributed to the claimed invention with clear and convincing evidence. See Hess v. Advanced Cardiovascular Sys., Inc., 106 F.3d 976, 980 (Fed. Cir. 1997). The district court's findings demonstrate that under the correct legal test, Vanderbilt did not carry its burden. Thus, any erroneous interpretations of our case law were harmless error.

COSTS

No costs.

AFFIRMED

DYK, Circuit Judge, concurring in part and dissenting in part.

There is no question that the district court applied the wrong standard for joint inventorship. The majority agrees, and I agree. However, I respectfully dissent from the majority's conclusion that the district court's legal error was harmless, because in my view, the findings are either contradictory or infected by the court's legal error. I would vacate the judgment and remand, requiring the district court to make findings of fact in light of the correct law.

I

Vanderbilt University ("Vanderbilt") argues that its scientists—Drs. Jackie D. Corbin, Sharron H. Francis, and Sekhar R. Konjeti ("the Vanderbilt scientists")—should be added as joint inventors to the patents in suit under two theories: (1) Dr. Richard Labaudiniere ("Labaudiniere") at Glaxo, Inc. ("Glaxo") used the Vanderbilt scientists' disclosure of 8-(4-hydroxy phenylthio)-IBMX to identify the compound GR30040x, which was in turn used by Dr. Alain Daugan ("Daugan"), the sole inventor listed on the patents in suit, and (2) Daugan used the Vanderbilt scientists' disclosure of 8-(4-hydroxy phenylthio)-IBMX to modify GR30040x and create the patented compounds. ICOS Corporation ("ICOS")[1] responds that the Vanderbilt scientists' disclosure played no role in Glaxo's identification of GR30040x or

[1] In 1991, Glaxo and ICOS entered into a collaboration agreement wherein all rights, title, and interest in the compounds ultimately covered by the patents in suit were assigned to ICOS.

the patented compounds. I agree with the majority that the district court's findings with respect to the second theory are not clearly erroneous. The court found that Daugan did not himself directly utilize the Vanderbilt scientists' contributions; this finding was supported by Daugan's testimony that he was not aware of the contributions and Labaudiniere's testimony that he did not forward the Vanderbilt scientists' work to Daugan.

However, the findings with respect to the first theory were either tainted by the district court's legal error or are contradictory on their face. The district court found that the Vanderbilt scientists did in fact make contributions to Glaxo's work, a point the majority ignores. After incorrectly explaining that the Vanderbilt scientists could not be joint inventors because there was no evidence that they had ever conceived the complete patented compound, the district court went on to state:

> This is not to say that Corbin, Francis and Konjeti did not make contributions to Daugan's inventive process; only that, under the applicable law, these contributions fall more into the category of "prosaic" contributions because they did not conceive the invention as claimed.

Vanderbilt Univ. v. ICOS Corp., 594 F. Supp. 2d 482, 505 (D. Del. 2009) (quoting Eli Lilly & Co. v. Aradigm Corp., 376 F.3d 1352, 1358–59 (Fed. Cir. 2004)) (emphases added). The district court also found that ICOS's position that Glaxo made no use of the Vanderbilt scientists' disclosures was "untenable." Id. at 505–06. It further stated that ICOS "loses

credibility in the court's view for failing to acknowledge that Glaxo made any use of plaintiff's disclosure." Id. at 506. The court even cited a number of factors supporting its finding that Glaxo relied on the Vanderbilt scientists' work in Glaxo's research: the disclosed potency of 8-(4-hydroxy phenylthio)-IBMX, the common structure of the compounds, and the short time between the Vanderbilt disclosure and Glaxo's identification of GR30040x. Id. at 505–06.

At the same time, the district court found that ICOS's theory as to how Labaudiniere identified GR30040x was unsupported. Prior to trial, ICOS asserted that Labaudiniere identified GR30040x by following up on research reported in two journal articles. Id. at 496. But after it was shown that one of those articles was not published until after GR30040x had been tested, ICOS offered a different story at trial. ICOS claimed that Labaudiniere arrived at GR30040x by performing substructure searches based on the tetrahydro beta-carboline fragment of GR35273, a compound discovered in a separate Glaxo program. See id. at 497–98. However, the district court noted that "nowhere in its papers did [ICOS] articulate why Labaudiniere selected tetrahydro beta-carbolines (more specifically, the tetrahydro beta-carboline fragment of GR35273) for his substructure searches." Id. at 506.

Thus the district court found that the Vanderbilt scientists did make a contribution to the identification of GR30040x. The district court then went on to find that "[Vanderbilt]'s theory (which is devoid of evidence regarding the alleged substructure searches based on 8-(4-OH-PT)-IMBX [sic]) and [ICOS]'s story (which is devoid of the aforementioned foundation) [are] equally

plausible with respect to the identification of GR30040x." Id. at 506 (emphasis added). As a footnote to this finding, the district court added: "Notably, even if GR30040x were the invention, the balance would not so tip in favor of plaintiff such as to constitute clear and convincing evidence." Id. at 506 n.53.

II

There are two possible ways to interpret the district court's findings, either of which requires a remand. The first is that the district court's findings are directly contradictory. The court could not have properly found that the Vanderbilt scientists made a contribution to the identification of GR30040x if it were "equally plausible" that they did not make a contribution. In this situation, we must send the case back to the district court so that it can reconsider its findings. Both this circuit and other circuits have uniformly found that judgments based on contradictory findings cannot stand. See, e.g., Essex Electro Eng'rs, Inc. v. Danzig, 224 F.3d 1283, 1295 (Fed. Cir. 2000); Mattson v. Dep't of Treasury, 86 F.3d 211, 215 (Fed. Cir. 1996); Lyles v. United States, 759 F.2d 941, 944 (D.C. Cir. 1985); Grano v. Dep't of Dev. of City of Columbus, 637 F.2d 1073, 1081–82 (6th Cir. 1980); Legate v. Maloney, 334 F.2d 704, 708 (1st Cir. 1964).

The alternative is that the district court found that Vanderbilt did not establish by clear and convincing evidence that the Vanderbilt scientists' contributions were sufficient to make them joint inventors. The problem with this interpretation of the finding is that it is obviously tainted by the district court's view that in order to be joint inventors, the Vanderbilt scientists

must have "conceived the 'specific chemical structure of the compound' claimed or 'the compound with all of its components,' or communicated that compound to Glaxo." Vanderbilt, 594 F. Supp. 2d at 505 (citations omitted). In particular, the district court misinterpreted our decision in American Bioscience when it stated that the Vanderbilt scientists could not be joint inventors "even if the court were to find that [their] disclosure of 8-(4-OH-PT)-IMBX [sic] led to the identification of GR30040x and the subsequent discovery of [the patented compounds]" because "the contribution of a molecular scaffold in the context of one molecule . . . [could not] render[] the disclosing party or parties [joint] inventors of a different family of molecules containing the same scaffold." Id. at 506–07; see Bd. of Educ. ex rel. Bd. of Trustees of Fla. State Univ. v. Am. BioScience, Inc., 333 F.3d 1330 (Fed. Cir. 2003). The majority correctly rejected this legal error. See Majority Op. at 19.

An alleged joint inventor does not have to conceive of the entire claimed invention, as the district court mistakenly required. He merely must contribute to the conception of the claimed invention. Eli Lilly, 376 F.3d at 1359. There is "no explicit lower limit on the quantum or quality of inventive contribution required for a person to qualify as a joint inventor." Fina Oil & Chem. Co. v. Ewen, 123 F.3d 1466, 1473 (Fed. Cir. 1997). The law does not require that the joint inventors physically work together or at the same time, or each make the same level of contribution. 35 U.S.C. § 116; see also Kimberly-Clark Corp. v. Procter & Gamble Distrib. Co., 973 F.2d 911, 917 (Fed. Cir. 1992) (providing "one inventor seeing a relevant report and building upon it" as an example of joint inventive effort). A joint inventor need only "make a contribution

to the conception of the claimed invention that is not insignificant in quality, when that contribution is measured against the dimension of the full invention." Fina Oil, 123 F.3d at 1473. While the district court found that the Vanderbilt scientists made some contribution, it has not told us exactly what that contribution was or why that contribution was not enough to make the Vanderbilt scientists joint inventors under the correct standard. If the Vanderbilt scientists made contributions, as the district court found, the fact that those contributions may not have been "appropriated by Dr. Labaudiniere for his substructure search," Majority Op. at 15, does not foreclose the possibility that the Vanderbilt scientists' contribution was sufficient to make them joint inventors.

Because the district court's findings were either contradictory or tainted by legal error, I think we must vacate the judgment of the district court and remand in order that the court may make factual findings under the proper law. I dissent from the majority's decision to affirm what I view as an untenable district court decision.

APPENDIX B

IN THE UNITED STATES DISTRICT COURT FOR THE DISTRICT OF DELAWARE

Civ. No. 05-506-SLR

[Filed January 27, 2009]

VANDERBILT UNIVERSITY,)
)
Plaintiff,)
)
v.)
)
ICOS CORPORATION,)
)
Defendant.)

Vincent A. Bifferato, Jr., Esquire, Ian Connor Bifferato, Esquire, and Raj Srovatsan, Esquire of Bifferato Gentilotti LLC, Wilmington, Delaware. Counsel for Plaintiff. Of Counsel: Kurt C. Rommel, Esquire of Miles & Stockbridge P.C., McLean, Virginia; Robert S. Brennen, Esquire and Donald E. English, Jr., Esquire of Miles & Stockbridge P.C., Baltimore, Maryland.

Richard K. Hermann, Esquire and Mary B. Matterer, Esquire of Morris James LLP, Wilmington, Delaware. Counsel for Defendant. Of Counsel: Kevin M. Flowers, Esquire, Thomas I. Ross, Esquire, and

Matthew C. Nielsen, Esquire of Marshall, Gerstein & Borun LLP, Chicago, Illinois.

OPINION

Dated: January 27, 2009
Wilmington, Delaware

/s/ Sue L. Robinson
ROBINSON, District Judge

I. INTRODUCTION

Plaintiff Vanderbilt University ("plaintiff" or "Vanderbilt") brought the present action pursuant to 35 U.S.C. § 256 against defendant ICOS Corporation ("defendant" or "ICOS") on July 20, 2005, requesting that the court direct the United States Patent and Trademark Office ("PTO") to correct U.S. Patent Nos. 5,859,006 ("the '006 patent") and 6,140,329 ("the '329 patent") by adding three Vanderbilt professors as inventors. (D.I. 1) A bench trial was held between January 7, 2008 and January 15, 2008 on the issues of inventorship of the '006 and '329 patents. Post-trial briefing has been completed. (D.I. 153, 150, 154) The court has jurisdiction pursuant to 28 U.S.C. §§ 1331 and 1338. Having considered the documentary evidence and testimony, the court makes the following findings of fact and conclusions of law pursuant to Fed. R. Civ. P. 52(a).

II. FINDINGS OF FACT AND CONCLUSIONS OF LAW[1]

A. The Parties

1. Vanderbilt is a Tennessee not-for-profit corporation with its principal place of business in Nashville, Tennessee. (D.I. 130, ex. 1 at ¶ 1) Vanderbilt brought this action pursuant to 35 U.S.C. § 256, requesting that the court add Jackie D. Corbin, Ph.D., Sharron H. Francis, Ph.D., and Sekhar R. Konjeti, Ph.D. as inventors on the '006 and '329 patents. (D.I. 1) All three scientists are employed as professors at Vanderbilt and, consistent with their terms of employment, have assigned all rights that they may have in the '006 or '329 patents to Vanderbilt. (PTX-6; PTX-7; PTX-8)

2. ICOS is a Delaware corporation with its principal place of business in Bothell, Washington.[2] (*Id.* at ¶ 2) ICOS is the owner by assignment of the '006 and '329 patents (together, the "patents at issue").

3. Glaxo Wellcome Inc. is a North Carolina corporation (hereinafter, "Glaxo").[3] Glaxo Group

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[1] The court is appreciative of ICOS' counsel's submission of DVDs containing the parties' post-trial briefs and exhibits in searchable, hyperlinked format.

[2] ICOS was acquired by Eli Lilly and Company on January 29, 2007; it is now a wholly-owned subsidiary of that company. (D.I. 130, ex. 1 at ¶ 3)

[3] In 2001, Glaxo merged with SmithKline Beecham to form Glaxo SmithKline.

Limited is Glaxo's English subsidiary (hereinafter, "Glaxo U.K."). In 1991, Glaxo[4] and Glaxo U.K. entered into a collaboration with ICOS, assigning to ICOS the rights, title, and interest in the compounds covered by the patents at issue. (PTX-406) At all times relevant to the present litigation, Glaxo maintained a research facility in Les Ulis, France (hereinafter, "Glaxo France").

B. The Technology at Issue

4. Cyclic guanosine monophosphate ("cGMP") is a chemical messenger in the body that activates cGMP kinase,[5] resulting in the relaxation of smooth muscle tissue. The relaxation of vascular smooth muscles lead to vasodilation[6] and increased blood flow. (103:5-23) Phosphodiesterase-5 ("PDE5") is an enzyme that breaks down cGMP. (Tr. 103:4-5) PDE5 has two different binding sites: one for binding cGMP to regulate it, and another for binding cGMP to break it down. (D.I. 140 at 115:20-116:24) Phosphodiesterase (or "PDE") inhibitors prevent the degradation of cGMP, thereby enhancing and/or prolonging smooth muscle relaxation.

5. The '006 patent claims at issue (claims 1-8, 10, 12 and 13) are directed to chemical compounds and

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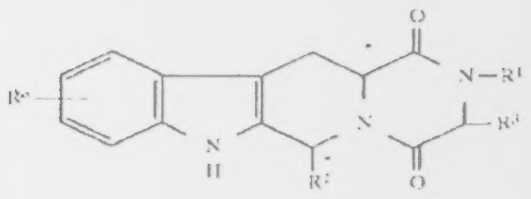
[4] At that time, Glaxo Wellcome's predecessor, Glaxo, Inc.

[5] Also called protein kinase G or PKG. Generally, kinases are enzymes that phosphorylate particular target molecules. Protein kinases act on and modify the activity of proteins.

[6] Generally, the widening of blood vessels, resulting from relaxation of smooth muscle cells within the vessel walls.

methods for making those compounds. The compounds are tetracyclic derivatives of the following general structure:

A compound of formula (I)

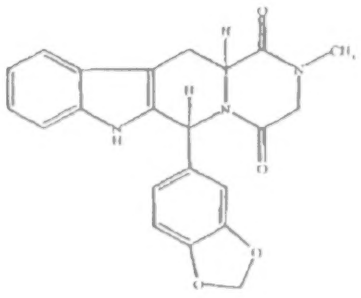


The '006 patent provides that such compounds are "potent and selective inhibitors of cyclic guanosine 3',5'-monophosphate specific phosphodiesterase (cGMP specific PDE)." ('006 patent, col. 1, ll. 8-12)

6. The '006 patent teaches that PDE5 inhibition caused by the claimed compounds results in elevated cGMP levels, resulting in, amongst other benefits, improved vasodilation. ('006 patent, col. 5, ll. 15-35) Such compounds are of interest "for the treatment of a variety of conditions where inhibition of [PDE5] is thought to be beneficial," for example, the treatment of cardiovascular disorders. ('006 patent, col. 1, ll. 12-15; col. 5, ll. 9-14)

7. The '329 patent claims at issue (1, 2, 3, 5-12, and 15-21) are directed to compositions and methods of treating impotence, also called erectile dysfunction ("ED"), in a male animal involving the administration of at least one of the compounds claimed in the '006

patent. One such compound is "tadalafil,"[7] the active ingredient in the prescription ED drug Cialis®. Tadalafil has the following structural formula:



C. Nature of the Dispute

8. Plaintiff asserts that Corbin, Francis and Konjeti conceived of a compound, 8-(4-hydroxy phenylthio)-IMBX (also referred to as 8-(4-OH-PT)-IMBX), which was communicated to Glaxo in 1992 pursuant to a research agreement. According to plaintiff, the disclosure of 8-(4-OH-PT)-IMBX led to Glaxo's development of two molecules incorporating the same molecular scaffold and, ultimately, the general chemical structure of formula 1 of the '006 and '329 patents.

9. Glaxo scientist Dr. Alain Daugan, who began work on Glaxo's PDE inhibitor project in June 1992, is the sole named inventor on the '006 and '329 patents. Defendant asserts that Daughan independently

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[7] Tadalafil has the formula $C_{22}H_{19}N_3O_4$ and IUPAC name (6R-trans)-6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-pyrazino [1',2':1,6] pyrido[3,4-b]indole-1,4-dione.

conceived the claimed compounds by conducting a comprehensive medicinal chemistry study between June 1992 and January 1994.

D. Legal Framework

10. 35 U.S.C. § 116 provides that "[w]hen an invention is made by two or more persons jointly, they shall apply for a patent jointly and each make the required oath, except as otherwise provided in this title. Inventors may apply for a patent jointly even though (1) they did not physically work together or at the same time, (2) each did not make the same type or amount of contribution, or (3) each did not make a contribution to the subject matter of every claim of the patent."

> All that is required of a joint inventor is that he or she (1) contribute in some significant manner to the conception or reduction to practice of the invention, (2) make a contribution to the claimed invention that is not insignificant in quality, when that contribution is measured against the dimension of the full invention, and (3) do more than merely explain to the real inventors well-known concepts and/or the current state of the art.

Pannu v. Iolab Corp., 155 F.3d 1344, 1351 (Fed. Cir. 1998). Section 116 "sets no explicit lower limit on the quantum or quality of inventive contribution required for a person to qualify as a joint inventor. Rather, a joint invention is simply the product of a collaboration between two or more persons working together to solve the problem addressed." *Fina Oil and Chem. Co. v. Ewen*, 123 F.3d 1466, 1473 (Fed. Cir. 1997) (citing

Burroughs Wellcome Co. v. Barr Labs., Inc., 40 F.3d 1223, 1227 (Fed. Cir. 1994)).

11. "A patent is invalid if more or fewer than the true inventors are named." *Gemstar-TV Guide Intern., Inc. v. Int'l Trade Com'n*, 383 F.3d 1352, 1381 (Fed. Cir. 2004) (citing *Jamesbury Corp. v. United States*, 518 F.2d 1384, 1395 (Ct. Cl. 1975)); 35 U.S.C. § 102(f) ("A person shall be entitled to a patent unless . . . he did not himself invent the subject matter sought to be patented[.]") Because patents are presumed valid, 35 U.S.C. § 282, there is a presumption that the named inventors on a patent are the true inventors. *Gemstar*, 383 F.3d at 1381 (citation omitted). This presumption may be overcome by demonstrating, by clear and convincing evidence, that the alleged omitted inventor "contribute[d] in some significant manner to the conception of the invention" claimed. *Id.* (quoting *Fina Oil & Chem. Co. v. Ewen*, 123 F.3d 1466, 1473 (Fed. Cir. 1997)).

12. 35 U.S.C. § 256 provides that an error in naming persons who are not inventors or in omitting inventors will not invalidate a patent where a correction is requested (and approved by) the PTO Director, or where "[t]he court before which such matter is called in question [orders] correction of the patent on notice or hearing of all parties concerned[.]" Plaintiff at bar does not seek to invalidate the '006 and '329 patents, but seeks an order directing the Director of the PTO to correct the named inventorship. (D.I. 153 at 50) Regardless of the relief requested, Corbin, Francis, and Konjeti must establish their

co-inventorship by facts supported by clear and convincing evidence.[8] See *Gemstar*, 383 F.3d at 1382.

E. Inventorship Evidence

The court turns now to the findings of fact upon which its ultimate conclusion on inventorship will be based.

1. Pre-collaboration

13. Corbin and Francis have been professors of molecular physiology at Vanderbilt University School of Medicine since the 1970s. Their research focuses on the molecular aspects of smooth muscle relaxation. Francis specifically focuses on cGMP. Corbin and Francis identified PDE5 in the late-1970s. (D.I. 140 at 115:20-116:24)

14. Prior to their collaboration with Glaxo, Corbin and Francis tested several dozen cGMP analogs. (PTX-35 at VM601; D.I. 140 at 133:9-10) They discovered that there were two forms of cGMP kinase, type Iα and Iβ. (D.I. 140 at 133:17-19)

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[8] Despite plaintiff's invitation to apply a lesser standard in view of the fact that the PTO does not verify named inventors, the court declines to apply a preponderance of the evidence standard absent compelling Federal Circuit authority.

2. Plaintiff's cGMP analog work & the communication of 8-(4-OH-PT)-IMBX to Glaxo

15. On December 16, 1988, Corbin completed an application for a "Glaxo Cardiovascular Discovery Grant." (PTX-32) Along with this application, Corbin and Francis submitted an abstract of their research proposal and the research proposal itself (hereinafter, "the 1988 Research Proposal"). (PTX-35)

16. The objective of the 1988 Research Proposal was described as "develop[ing] cGMP analogs[9], or combinations of analogs, that are potent and specific, and that exhibit an appropriate pattern of reversibility or persistence, in causing relaxation of vascular smooth muscle[.]" (PTX-35, ex. A, p. 10 at VM599) New cGMP analogs would be tested for their activation "of smooth muscle type Iα and Iβ isozymes[10] of cGMP kinase," which isozymes have two specific cGMP binding sites ("site 1 and 2"). (*Id.*) In other words, the team sought to identify compounds that would activate cGMP kinase, just like cGMP would activate cGMP kinase to achieve smooth muscle relaxation, therefore mimicking an increase in cGMP.[11] The proposal

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[9] A compound that is similar in structure to cGMP.

[10] Generally, enzyme variants having different amino acid sequences but which catalyze the same chemical reaction (*i.e.*, have the same function).

[11] In this regard, the "focus" would be on four analog groups: "(a) analogs that are selective for cGMP-binding site 1 of cGMP kinase; (b) analogs that are selective for site 2; (c) analogs that bind with high affinity to both sites; and (d) analogs that are

provided that combinations of cGMP analogs and specific cGMP PDE inhibitors would be tested for synergistic effects. (*Id.* at VM599) Also included was a list of the new cGMP analogs that had been synthesized by Corbin and Francis: 8-pCL-phenyl-S-cGMP, a compound with an eight-position substitution, as well as several other 8-substituted compounds (e.g., compound GI118611A). (*Id.* at VM601; D.I. 143 at 651:23-652:11)

17. Corbin was selected for a Glaxo Cardiovascular Discovery Grant. Following a visit from Glaxo representatives, plaintiff and Glaxo executed a "Glaxo Cardiovascular Discovery Grants Research Agreement" (hereinafter, "the 1989 Research Agreement") dated July 1, 1989. (PTX-35) The 1988 Research Proposal (and abstract of that agreement) became appendices to the 1989 Research Agreement.

18. The 1989 Research Agreement provided that the project would be funded for a three-year period, and contemplated renewal by mutual agreement of all of the parties. (*Id.* at 2-3) Any inventions made by a participant in the project "and conceived or reduced to practice during the course of and under the project shall be the property of the University subject to the rights agreed herein to be granted to Glaxo under a license agreement to be entered into between the parties." (*Id.* at 3-4) Glaxo retained the right to delay publication and dissemination of the results of plaintiff's work relating to the Agreement for up to

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persistent in causing relaxation of artery strips." (PTX-35, ex. A, p. 10 at VM600)

three months if Glaxo believed the publication would jeopardize its patent rights. (*Id.* at 12)

19. On November 1, 1989, Corbin presented his group's work to a group of senior Glaxo scientists in North Carolina: Dr. Crist Frangakis, Joel Shaffer, Jeff Wiseman, and Dr. Thomas Rimele. (PTX-37)

20. In January 1990, Konjeti joined the Vanderbilt lab as a postdoctoral fellow to collaborate with Corbin and Francis on cGMP analogs under the 1989 Research Agreement. (647:2-8) Konjeti studied Corbin and Francis's work on cGMP and PDE5 upon his arrival, as well as the research proposal, to familiarize himself with their work. (647:23-648:5)

21. From March 22 to 24, 1990, by the invitation of Dr. Don Kirksey, Director of Glaxo's "Discovery Program," Corbin attended a "Cardiovascular Discovery Conference" in Tucson, Arizona. (D.I. 140 at 134:19-135:4; PTX-36) During the conference, Corbin had a lunch meeting with several scientists: Dr. Joseph Beavo (from the University of Washington ("UW")) and Kirksey, Shaffer, Rimele and Wiseman (all from Glaxo). (PTX-42) The parties discussed a potential collaboration between plaintiff and UW to determine the DNA sequence for and ultimately clone PDE5.[12] (*Id.*)

22. Aside from doing work under the 1989 Research Agreement, Corbin and Francis continued their work on PDE5 during this period, funded by the National

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[12] Cloning PDE5 would avoid the process of purifying PDE5 from rat and cow lung for testing purposes. (D.I. 140 at 139:24-140:24)

Institutes of Health. (D.I. 140 at 141:7-143:5) An article received for publication in the Journal of Biological Chemistry on April 11, 1990 describes Corbin and Francis's purification of PDE5 from cow lung.[13] (PTX-43) This work illustrated that zaprinast[14] was a PDE5 inhibitor. (D.I. 140 at 141:24-142:2) According to Corbin, these results got the team thinking that "the studies of cyclic GMP analogs on [cGMP kinase] that we had already done might apply to PDE5." (*Id.* at 142:7-14)

23. Following the 1990 Cardiovascular Discovery Conference, Corbin, Francis and Konjeti submitted a progress report to Glaxo on work done under the 1989 Research Agreement, entitled "Cardiovascular Discovery Grant 1989-1990 Annual Report" (hereinafter, "the 1990 Progress Report").[15] (PTX-44) The 1990 Progress Report listed newly synthesized cGMP analogs that were tested over the past year for activation of cGMP kinase (both types I[alpha] and I[beta]), including: 8-napthylthio-cGMP, 8-o-Br-PT -cGMP, and 8-p-OH-PT-cGMP. (*Id.* at VC-78) The 1990 Progress Report stated that "[i]t should be noted that

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[13] This PDE5 work was also published in 1990 as a book chapter entitled "Cyclic Nucleotide Phosphodiesterases: Structure, Regulation and Drug Action." (PTX-420; D.I. 143 at 779:7-14)

Also named on both publications is Melissa K. Thomas, a graduate student at Vanderbilt University.

[14] 1,4-Dihydro-5-(2-propoxyphenyl)-7H-1,2,3-triazolo[4,5-d] pyrimidine-7-one. A compound originally developed as an anti-allergy treatment.

[15] Defendant does not contest plaintiff's representation that the 1990 Progress Report was presented following the Cardiovascular Discovery Conference in 1990.

the most potent smooth muscle relaxants, 8-Br-PET-cGMP and 8-pOH-PT-cGMP, are ~20 times more potent than the best cGMP analog (8-pCL-PT-cGMP) tested prior to this study." (*Id.* at VC-79)

24. On November 28, 1990, Corbin sent Kirksey at Glaxo U.K.[16] a copy of an abstract he sought to be published at a Federation of American Societies for Experimental Biology ("FASEB") conference scheduled in 1991 (hereinafter, the "FASEB abstract"). (PTX-47) The results contained in the FASEB abstract included the discovery that the potency of the cGMP analogs with certain functional groups attached at the 8-position was enhanced by the attachment of electron-donating groups to the phenyl ring. (*Id.*) ("Analogs modified with a derivatized phenyl-activating group at the 8-position were 100-1000 fold more potent in activating [cGMP kinase type Iα] than [cGMP kinase type Iβ]). Electron donating substituents such as OH, NH2 and OCH3 on the phenyl ring enhanced the potencies of these analogs in activating [type Iα]."]) Corbin testified that Glaxo required him to withdraw the FASEB abstract. (150:11-12)

25. On March 18, 1991, Corbin made a presentation at the "Glaxo Discovery Conference" in North Carolina on his team's progress to date. (PTX-53) In attendance were Kirksey (Glaxo), Beavo (UW), two Glaxo

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[16] On October 23, 1990, Glaxo informed Corbin that the administration of Glaxo's cardiovascular program was being transferred from North Carolina to Glaxo Group Research ("GGR") in the United Kingdom. (PTX-45)

scientists from the United Kingdom (Barry Moss, Mike Drew), and several others. (*Id.*; D.I. 140 at 151:7-25)

26. Also on March 18, 1991, Rimele authored a "Cardiovascular Status Report" (hereinafter, the "Glaxo CSR") detailing the history and results of Glaxo's research in the area of smooth muscle relaxation. (PTX-51) The Glaxo CSR states that the first examples of cGMP analogs were submitted in May 1990. (*Id.* at GLAX15564) Testing on these analogs began in June 1990. (*Id.*) Among the list of cGMP analogs was GI118611A, Glaxo's designation for 8-(4-chloro-phenylthio)-cGMP, a compound previously listed by plaintiff in the research proposal portion of the 1989 Research Agreement. (*Id.* & GLAX15570; D.I. 143 at 651:22-652:10) In addition to GI118611A, the Glaxo CSR lists four additional cGMP analogs that had been included in either the 1989 Research Agreement or the 1990 Progress Report: (1) GI 120446A, or 1-napthylthio cGMP (D.I. 143 at 652:12-653:12; PTX-51 at GLAX15571; PTX-35 at VM-602[17]); (2) GI 118815A, or napthylthio cGMP; (3) GI 119889A, or 8-octobromo cGMP (D.I. 143 at 653:13-654:1; PTX-51 at GLAX15570; PTX-40 at VK347[18]); and (4) GI 120547A, a hydroxythio cGMP[19]

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[17] The research proposal of the Agreement notes that "[t]he more bulky 1-napthyl-S-cGMP (analog 14) will be made by using 1-napthylenethiol as starting material."

[18] Konjeti's lab notebook lists 8-napthylthio cGMP and 8-octobromo cGMP as compounds synthesized as of February 13, 1990. (PTX-40 at VK-347; D.I. 143 at 649:12-650:6)

[19] Because the precise nomenclature of this compound does not appear to be of record, the court cannot match up GI 120547A

(D.I. 143 at 654:2-654:22; PTX-51 at GLAC15621).[20] Zaprinast and a compound SC-44238 were listed as cGMP PDE inhibitors, and IMBX, caffeine, and theophyline were listed as nonselective inhibitors. (PTX-51 at GLAX15632)

27. The Glaxo CSR described the progress on cGMP analogs, discussed at a May 4, 1990 meeting, as follows:

> The important interactions of the protein with cGMP were presented along with the location of a novel lipophilic binding pocket off of the eight position of the guanine base. This modeling will serve as the basis to design novel cGMP analogs to synthesize.

(*Id.* at GLAX15594; *see also id.* at GLAX15596 ("Based upon the location of a novel lipophilic binding pocket off the eight position of the guanine base, compounds with bulky groups off the 8-position are being synthesized.")).

28. The Glaxo CSR described future work regarding PDE5 as: (1) continu[ing to] develop an SAR of

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with the 1990 Progress Report as per Konjeti's testimony. Defendant, however, did not contest this point in its answering brief.

[20] Glaxo patent counsel conducted a literature search in April 1991, and concluded that several of these compounds were not previously described. (PTX-57) It is unclear from the record exactly which compounds were deemed novel as of that date.

zaprinast[21]; (2) synthesiz[ing] compounds that vary the distance of a particular zaprinast; (3) synthesiz[ing] a substrate for an affinity column for PDE5; (4) develop[ing] syntheses of zaprinast-cGMP hybrids; and (5) validat[ing] the cGMP PDE enzyme assay. (PTX-35 at GLAX15597)

29. In April 1991, Corbin and his group sent a minuscript for Glaxo's approval for publication, entitled "Relaxation of Pig Coronary Arteries by New and Potent cGMP Analogs that Selectively Activate Type Iα Compared to Type Iβ cGMP-Dependent Protein Kinase."[22] (PTX-56) In the article, Corbin et al. hypothesized that the potency of 8-position substituted cGMP analogs was due to the "spacial tolerance of large substituents at C-8, preference of this binding site for the syn[23] conformation of cyclic nucleotides and the electron-withdrawing/donating properties of

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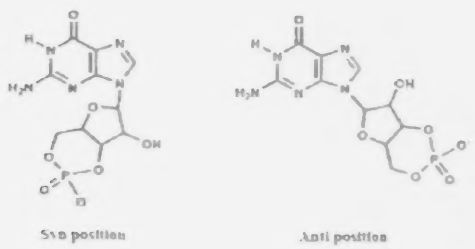
[21] A weak PDE inhibitor known at the time.

[22] This paper was eventually published in 1992. (D.I. 140 at 163:5-8)

[23] cGMP has two segments which can rotate around a specific point of the molecule, resulting in two 3-D configurations. When cGMP is in the "syn" position, the guanine moiety and the ribose cyclic phosphate moiety are pointed in the same direction. In the "anti" position, the two moieties are turned away from each other.



Syn position Anti position

the substituent." (*Id.* at VC-146) "It was thus concluded that a bulky halogen substituent with low electron withdrawing power favors the activation of the cGMP kinases." (*Id.*) Corbin testified that analogs with large bulky groups at the 8-position are fixed in the syn position; they cannot rotate to the anti position due to the substituent. (D.I. 140 at 163:9-165:1)

30. On May 29, 1991, Dr. M. W. Elwes of Glaxo's External Scientific Affairs Division, Glaxo U.K., sent Corbin a letter stating the following:

> [Glaxo has] now had time to examine the projects in [ ] light of our new arrangements for supervision of the cardiovascular therapeutic area within the Glaxo research organization. As you will be aware responsibility for this therapeutic area now rests with Glaxo Group research and our CVS Research Management Committee (RMC) is not lead by Dr. Barry Ross. . . . We consider your work to be very close to our own project interests and so we would like to develop as close a collaboration with you as geography will allow for the remaining period of the grant. I would ask you, therefore, to send your reports in the future to Dr. Fiona Roberts, our Academic Liason Manager, at this [U.K.] address. . . .

(PTX-59A)

31. Corbin testified that he and Glaxo representatives engaged in informal discussions during that time regarding the continuation of plaintiff's grant. (D.I. 140 at 171:8-172:20) During these discussions, Glaxo indicated a potential

bioavailability issue insofar as cGMP breaks down in the stomach and intestines, never reaching its destination tissue. (*Id.*) According to Corbin, Glaxo also indicated that future work should focus more on PDE5 than the original grant did. (*Id.*)

32. Corbin responded to Elwes' letter on July 24, 1991, in which he noted that he was pleased with Glaxo's interest in plaintiff's work, and that it "seems [from previous informal discussions with Glaxo representatives] that any future relationship with Glaxo, following the award termination, would be an open-ended proposition." (PTX-71) Corbin asked to be informed "if there is anything [he] could do now to improve the chances for such a continuation . . . We feel that this particular project is going quite well, and we wish to carry on with it if possible." (*Id.*)

33. Glaxo meeting minutes for the "PDE Project" dated June 3, 1991 state that Glaxo's goal at that time was "[t]o discover a potent specific inhibitor of cGMP-specific ('type V') [PDE] for the treatment of hypertension, angina pectoris, etc." (PTX-62) Some specific "molecules already obtained in the U.S., with some biological results," were "azapurines" and "imidazoles."[24] (*Id.*) Action items included "search[ing] for available molecules." (*Id.*) "The compound that seems to be the most interesting at this point is AH19041xx (azapurine family . . .)." (*Id.*) The following "[o]ther molecules to be studied (various vasodilators and PDE inhibitors" were listed:

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[24] Generally, imidazole is a organic compound with the formula $HC_3H_3N_2$. Purine is a heterocycle consisting of a pyrimidine ring fused to an imidazole ring. Azopurines are purine analogs.

hydralazine, dihydralazine, cudralazine, minoxidil, pinacidil, diazoxide, flosequinan, nicotinamide ethers, nitraquazone, imidazolidinones, rolipram analogs, and cicletanine. (*Id.*)

34. From June 17-20, 1991, Dr. Jorge Kirilovsky, a scientist with Glaxo France, traveled to North Carolina for meetings with Rimele, Domanico, and other Glaxo scientists regarding PDE V.[25] (PTX-58; PTX-58A) Glaxo sent compounds listed in the meeting minutes of June 3, 1991 to Glaxo France. (*Id.*; D.I. 142 at 474:20-475:3, 478:12-19) The American scientists proposed to test "AH19041X-type imidazoles fairly soon" to determine any effects on the central nervous system. (PTX-58A at GLAX15734; D.I. 142 at 477:3-8) Glaxo was in discussions with ICOS at this time, which was to clone and express about 30 enzymes which would be used to test different types of compounds developed by Glaxo. "ICOS's priority would be type IV, followed by types V and III ." (PTX-58A at GLAXI5735-36)

35. Dr. Paul Grondin was hired by Glaxo in June 1991 by George Kirilovsky to carry out experiments for the PDE V project at Glaxo France; he was the first person assigned to do so. (D.I. 142 at 473:7-15, 474:1-4)

36. Minutes of a Glaxo France PDE Project meeting on July 9, 1991 reflect that

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[25] "Individuals who have been involved in the PDE V program in the past;" in addition, chemists David Uehling and Paul Feldman. (PTX-58A) Scientists Steve Simpson and Verghese were also listed in the memorandum discussing the trip. (*Id.*)

> [a] list of model compounds already characterized as PDE inhibitors has been drawn up on the basis of published work and the GI results. These compounds will be analyzed using the various tests currently being set up at Les Ulis: enzymology, isolated artery, isolated heart, whole animal.

The "proposed list of model compounds" for a "type V inhibitor" consisted of AH 91041XX, GI 122529X, and zaprinast. (PTX-69) "The second step will be to determine the lead compounds, drawing from either the PDE inhibitors presented in published work, the known vasodilators, or model compound analogs (above list)." (*Id.*)

37. The Glaxo July 1991 minutes state that a ChemBase computer file was set up to include all of the compounds tested and the results obtained. "Compounds of interest" GI 122529X and AH 19041XX were to be compared to zaprinast. (*Id.*) Neither compound was available in sufficient amounts at that time, and needed to be synthesized for the study. (*Id.*) Glaxo France's "[g]oal for the end of the year [1991]" was "[o]perational enzymology and pharmacology tests with in-house results on compounds chosen as references." (*Id.*)

38. Minutes of a Glaxo PDE Project meeting of August 27, 1991 reflect that Glaxo was, as of that date, "beginning [] in vivo testing of zaprinast and rolipram." (PTX-58A at GLAX15759) Dr. Bernard Dumaitre was planning to synthesize AH19041X as a reference compound, which was accomplished in September 1991. (PTX-58A; PTX-75) Compound GI122529X would not be available for six weeks, and

GI121730 was to be tested in its stead. (PTX-58A at GLAX15759) Finally, Glaxo noted an "action" item of "[i]mmediate synthesis of rolipram and denbuflyn" by Dumaitre and another scientist. (*Id.*)

39. A PDE Project meeting was held at Glaxo France on October 9, 1991. (JTX-7; PTX-77) At that time, Glaxo[26] was working to complete an assay to measure PDE5 inhibition. (D.I. 142 at 423:25-484:11) Following completion of the assay, Glaxo's objective was to "develop a specific tool of the zaprinast (asapurinone) type with 10 times greater activity." (*Id.*; PTX-77) Glaxo expected that in the near future, ICOS would possess a "type V [PDE] (human lung) . . . for screening." (PTX-77)

40. Also in October 1991, Corbin wrote Roberts at Glaxo requesting permission to provide plaintiff's "close collaborators" with the cGMP analogs "for basic research purposes." (PTX-81) Corbin indicated that Glaxo had approved, as of that date, "the publication of the syntheses and properties of the compounds." (JTX-43) Corbin testified that his request for a blanket approval to provide compounds to third parties was denied by Glaxo. (D.I. 140 at 175:4-6)

41. In November 1991, Corbin, Francis and Konjeti synthesized a new PDE5 inhibitor. (PTX-88 at VK-1737, 1757-62) IMBX was chosen as a parent compound for the new PDE5 inhibitor because it was known to work, it was cheap and readily available, and

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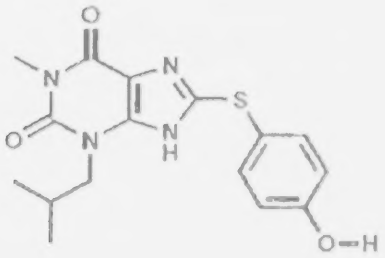
[26] Glaxo considered the PDE Project to be an international collaboration between Glaxo and Glaxo France. (PTX-77 ("The PDE project is international[.]"))

was easily substituted at the 8-position. (D.I. 140 at 185:4-17; D.I. 143 at 663:12-16, 786:2-21) A phenyl ring was attached to the 8-position of IMBX, and an electron-donating hydroxy group at the 4 position of that phenyl ring. The result was 8-(4-hydroxy phenylthio)-IMBX (or 8-(4-OH-PT)-IMBX), a potent PDE5 inhibitor.



42. Also in November 1991, Corbin drafted a letter to plaintiff's General Counsel, Jackie Schrago, with respect to Corbin's request for plaintiff to sponsor the compounds Corbin was developing. (PTX-89; D.I. 140 at 176:17-177:3) Corbin communicated to Schrago possible therapeutic uses for the new analogs, including the treatment of male impotence. (PTX-89) The treatment of ED with cGMP analogs had not been published in the literature as of this time. (D.I. 143 at 784:1-9, 796:8-25; D.I. 145 at 1139:9-17)

43. In December 1991, Dr. Richard Labaudiniere was hired by Glaxo France as the head of chemistry. (D.I. 141 at 392:10-393:23) Labaudiniere assumed leadership of the PDE5 project. (*Id.*) As head of chemistry, Labaudiniere was involved in all projects of that department and was responsible for discussing the best approaches for chemists' work, including suggesting modifications to compounds. Additionally, Labaudiniere was involved in management and

discussed methods of drug development with the head of biology. (*Id.*)

44. Also in December 1991, Corbin spoke with Ross at Glaxo U.K. about the possibility of extending plaintiff's collaboration with Glaxo. (D.I. 143 at 668:19-23, 784:20-785:10; PTX-41) On January 3, 1992, Corbin sent Ross a "general outline of a proposal for an extension of the Corbin/Glaxo corroboration (hereinafter, the "January 1992 general proposal"). (JTX-41) "The major change [of this proposal] is that it emphasize[d] a combined protein kinase/[PDE] approach[.]" (*Id.*) Corbin testified that the "major change" referenced was a focus on PDE5 inhibitors, at the encouragement of Glaxo scientists. (D.I. 140 at 178:17-179:23) Corbin theorized that "cyclic GMP analogs might apply to PDE5 as they applied to PKG" and, therefore, "[w]e could in practical terms even use the same analogs that we already synthesized for PKG to test on PDE5." (*Id.*)

45. The January 1992 general proposal contained three sections: cGMP analogs; "[i]nhibitors of a [cGMP]-binding [PDE]"; and "other projects to consider." (JTX-41) Regarding cGMP analogs, Corbin stated the following:

> We will expand on our most significant finding that analogs modified at the 1,2- and 8-positions of the guanine moiety of cyclic GMP are the most potent relaxants. We originally proposed to synthesize such analogs because 1,2-modified analogs bind to one cyclic GMP-binding site of the cG kinase and 8-modified analogs bind to the other site. As predicted, when these two structural elements

> were combined, the resulting compounds were even more efficacious because they bound well to both binding sites. We now believe that the high potencies of these analogs are due not only to the high kinase affinity of 1,2- and 8-modifications, but also to a strong [PDE] resistance due mainly to the 8-modifications. This latter property also contributes to the long-lasting analog effect observed in the intact tissue (and presumably in the intact organism). . . .

(JTX-41 at VC-225-26) Corbin testified that the "persistence" of the analogs, or failure to break down, was believed to be the result of resistence to PDE in the tissue. (D.I. 140 at 180:2-15)

46. With respect to PDE inhibitors, the January 1992 proposal stated the following:

> We will design [PDE] inhibitors based on the theory that the potencies of existing inhibitors, such as 3-isobutyl-1-methylxanthine (IMBX) and zaprinast, could be enhanced by appending groups that would allow the inhibitors to more closely resemble the entire cyclic GMP molecule. The existing inhibitors resemble only the guanine component. Our preliminary results indicate that this strategy works. **We have synthesized one compound that is about 160-fold more potent than the parent IMBX, and 6-fold more potent than the best existing inhibitor, zaprinast**. . . . This section overlaps neither with our NIH grant . . . nor with our ICOS/Glaxo collaboration described

> above. However, each of these projects should benefit from the others.

(JTX-41 at VC-226-27) (emphasis added) Corbin and Francis testified that they believed that compounds having both the guanine component and an appendage to make contact with the (exposed) ribose phosphate portion would be more potent. (D.I. 140 at 181:21-183:12; D.I. 143 at 790:3-792:9) Notably, Corbin and Francis did not have the genetic sequence of PDE5 at the time and did know the structure of the catalytic site; their theory was based upon observations of cGMP binding on PKG.[27] (791:23-794:11)

47. Finally, under the "other projects" heading of the January 1992 general proposal, Corbin noted that "the cG kinase has important disease-related functions other than the induction of vascular smooth muscle relaxation." (JTX-41 at VC-227) "Corpus cavernosum relaxation (male impotence)" was listed as an application of interest. (*Id.*) Corbin suggested Glaxo support plaintiff's research for three years starting in July 1992. (*Id.*)

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[27] That is, as explained in the FASEB abstract, hydrophobic groups of atoms, such as a phenyl ring, with additional electron-donating groups appeared to bind well to binding sites on PKG in the vicinity of the ribose phosphate moiety of cGMP. (PTX-47; D.I. 140 at 149:15-150:12) Francis acknowledged at trial that scientists at the time did not believe that PKG and PDE5 catalytic sites were related. She testified, however, that the team believed a relationship was "plausible" because a new PKG was developed in the lab that was identical in amino acid sequence but differed dramatically in affinity for cGMP, illustrating chemical preferences. (D.I. 143 at 793:4-794:11)

48. Glaxo was not researching male impotence in early 1992. (D.I. 141 at 407:12-24)

49. Ross flew from England for a presentation of the January 1992 general proposal on February 3, 1992. (JTX-42; D.I. 140 at 187:14-22; D.I. 142 at 583:10-19) On February 11, 1992, Glaxo France purchased a quantity of IMBX. (PTX-115)

50. On February 24, 1992, Corbin mailed Ross a final proposal including "[m]ore detail of the experimental design" with "increased emphasis on use of the newly synthesized compounds to study basic mechanisms of the protein kinase and [PDE]" (hereinafter, the "1992 Research Proposal").[28] (PTX-117; PTX-118) Like the January proposal, ,the 1992 Research Proposal specifically identified 8-(4-OH-PT)-IMBX as a new compound "that is about 160-fold more potent than the parent IMBX, and 6-fold more potent than the best existing inhibitor, zaprinast." (PTX-117 at 3) Other IMBX and zaprinast analogs were also listed. (*Id.* at 4; PTX-424) All but one had 8-position substitutions. (D.I. 143 at 672:3-6)

51. In addition, the 1992 Research Proposal stated that Corbin's team "now believe[d] that the high potencies of these analogs in intact tissues are not only due to the high kinase affinity of the 1,2- and 8-modifications, but also to a strong PDE resistance and antagonism due mainly to the 8-modifications." (PTX-117 at VC250) "[S]ome cGMP analogs are not only PDE-resistent, but they also act like

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[28] Corbin testified that he, Francis, and Konjeti jointly prepared the February 1992 proposal. (D.I. 140 at 190:22-24)

methylxanthine inhibitors of the enzyme by binding tightly to its catalytic site." (*Id.*)

52. On March 11 and 12, 1992, Glaxo tested 26 compounds for PDE5 inhibition, including a compound designated GR35273x, discussed in further detail *infra*. (DTX-IG at GLAX13202)

53. On April 8, 1992, Ross sent copes of the 1992 Research Proposal to six Glaxo scientists, including Dr. Francois Hyafil, head of the Glaxo France lab, and Labaudiniere. (PTX-121; D.I. 130, ex. 1 at ¶ 21) In his cover, Ross stated that Corbin's work on cGMP analogs and "prob[ing] the mechanism and role of smooth muscle protein kinases and [PDEs]" was "a substantial collaboration and the only one of the original US CV discovery grants that remains." (PTX-121) Further, Ross stated that

> Corbin is collaborating with the ICOS/Glaxo strategic alliance in the area of type V [PDE] enzyme mechanisms and function. This proposal is distinct from that collaboration and is primarily directed towards the cGMP simulated kinases. As a spinoff some compounds have demonstrated type V PDE inhibitory activity. Results eminating from this collaboration may provide the foundation for a future in-house discovery programme directed towards hypertension and congestive heart failure.

(*Id.*)

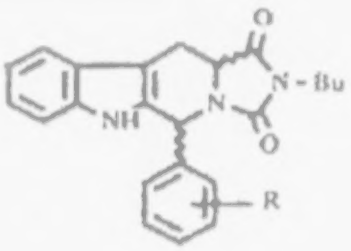
54. On April 23, 1992, Glaxo tested the PDE5 inhibitory capacities of 29 compounds. (PTX-425)

Among these were zaprinast, and a molecule designated GR30040x, discussed in detail *infra*. (PTX-140) There is no evidence of record demonstrating the date GR30040x was identified by Glaxo for the purpose of this testing.

55. Plaintiff asserts 11 of these 29 compounds contain what it calls the "Vanderbilt Structural Features," or "a 6-member ring fused to a 5-member ring, with some substitution at the 8-position." (D.I. 153 at 27)

3. The identification of GR30040x preceded the discovery of tadalafil

56. This case pivots around GR30040x, a beta-carboline[29] compound having the following four-ring scaffold structure.



(D.I. 150 at 11)

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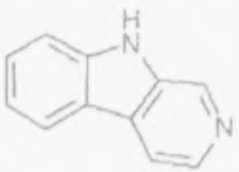
[29] Beta-carbolines are compounds comprising the following general (three-ringed) structure.



57. There is no dispute that Labaudiniere identified GR30040x as a "lead" compound for research regarding PDE5 inhibition. Following its identification, Daugan conducted research on GR30040x. Through the course of this research, Daugan discovered tadalafil.[30]

58. Plaintiff asserts that Labaudiniere used the "Vanderbilt Structural Features" for two purposes. First, plaintiff claims that the disclosure of 8-(4-OH-PT)-IMBX led to the discovery of the lead compound GR30040x. Second, plaintiff asserts that its disclosure of 8-(4-OH-PT)-IMBX contributed to the course of the modifications to GR30040x performed by Daugan.[31] The court addresses the facts relevant to each assertion in turn.

59. Plaintiff asserts that the "only logical source for the identification of GR30040x and the inclusion of the Vanderbilt Structural Features in the patented compounds" was the 1992 Research Proposal. (D.I. 154 at 12) To give context to plaintiff's claim, and in view of the presumption that Daugan invented the compositions and methods claimed in the patents at issue, the court first addresses Glaxo's evidence regarding how GR30040x was identified as the lead compound for Daugan's research.

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[30] The compounds of formula 1 of the patents at issue are beta-carboline/piperazinedione compounds; GR30040x and GF173321x are beta-carboline hydantoin compounds, and are not part of the claimed inventions.

[31] The parties debate the sequence of modifications to GR30040x performed by Daugan, as it relates to this argument.

a. Glaxo's evidence regarding the identification of GR30040x

i. Elgoyhen

60. In its pretrial disclosure, Glaxo asserted that Labaudiniere became aware in early 1992 of literature suggesting that beta-carbolines could alter cGMP levels, which caused him to use the "basic beta-carboline structure" of the prior art compounds to conduct a substructure search. (D.I. 130, pt. 4 at 3) When these compounds were tested, some were found to be fairly potent PDE5 inhibitors. Labaudiniere then asked Daugan to pursue the modification of these "lead compounds," including GR30040x. (*Id.*)

61. This theory is reflected in a paper received by the Journal of Medicinal Chemistry on February 5, 2003, entitled "The Discovery of Tadalafil: A Novel and Highly Selective PDE5 Inhibitor[.]" (hereinafter, the "Tadalafil Paper"). (JTX-29) As reflected in the Tadalafil Paper, "β-carbolines had been previously found to increase basal level of cGMP in rat cerebellum . . . [and] were also reported to inhibit crude rate aortic cyclic nucleotide [PDE] activity." Two references are cited: (1) a 1983 article in the European Journal of Pharmacology by B. Koe et al. entitled "Contrasting Effects of Ethyl β-Carboline-3-Carboxylate and Diazepam on Cerebellar Cyclic GMP Content and Antagonism of Both Effects by Ro 15-1788, A Specific Benzodiazepine Receptor Blocker" (hereinafter, "Koe"); and (2) a May 1992 article in the Journal of Pharmacology and Experimental Therapeutics by B. Elgoyhen et al. entitled "Relaxant Effects of β-Carbolines on Rat Aortic Rings" (hereinafter, "Elgoyhen"). (JTX-29 at ICOS737 & n. 10 & n.11) The

Tadalifil Paper proceeds to state that "[t]he β-carboine scaffold was then used as a basis for substructure searching in our internal database to find novel type 5 [PDE] inhibitors (chart 1)." (*Id.* at ICOS737)

62. Of record is a Glaxo document entitled "PDE V Inhibitors Project Annual Report for the Year Ending 30/4/93" (hereinafter, the "1992-93 Annual Report"). (DTX-P) The 1992-93 Annual Report reflects that Koe and/or Elgoyhen led Labaudiniere to beta-carbolines generally, while substructure searches on the tetrahydro beta-carboline portion of GR35273[32] led to the identification of GR30040x in particular:

> 4. 7. a- GR30040 analogues
>
> It is a new series of compounds we began to study last year starting from literature data on β-carboline and benzodiazepine derivatives having some vasorelaxant effect on precontracted rat aortic rings. These compounds displayed in our hand some PDE V inhibition activities. Substructure searches from β-CCE[33] and GR35273 on tetrahydro-β-carboline analogues in GLAX led to the idenfification of GR30040, a specific PDE V inhibitor, with activities similar to zaprinast (see figure 11). Studies have been performed to improve potency.

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[32] A beta-carboline compound. (D.I. 143 at 891:22-892:9)

[33] β-CCE or βCCE, chemical name ethyl beta-carboline-3-carboxylate (or beta-carboline-3-carboxylic acid ester), is a benzodiazepine antagonist and a member of the beta-carboline chemical family.

(*Id.* at GLAX00037)

63. Glaxo's internal testing record indicates that GR30040x was subjected to a 10 micromolar concentration test[34] on April 23, 1992, scoring an 86 for inhibition. (PTX-140) GR30040x was then tested to determine an IC_{50}[35] value on April 24, 1992, which revealed a value of 0.2 micromolar. (*Id.*) Tests on GR30040x using PDE1, or a type 1 PDE inhibitor, were performed on May 12 (10 micromolar concentration test) and June 3, 1992 (IC_{50} = 2.0 micromolar, a poor result). (*Id.*) Additional IC_{50} tests were performed on GR30040x (PDE5) on June 9 and 10, 1992 (IC_{50} = 0.6 and 0.15 micromolar, respectively). (*Id.*) A IC_{50} test was performed on βCCE on July 3, 1992, revealing a IC_{50} value of 0.8 micromolar. (PTX-170; D.I. 146 at 1215:18-1216:2)

64. Rafferty conceded that any searches conducted by Glaxo based on Elgoyhen or βCCE would have had to have occurred after Elgoyhen was published on May 8, 1992. (DTX-RJ; D.I. 146 at 1256:2-23) In short, GR30040x was not identified following Labaudiniere's reading of Elgoyhen.

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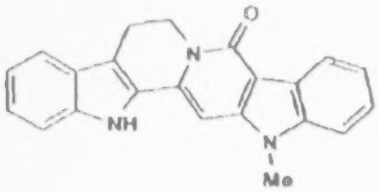
[34] Plaintiff represents that this test measures inhibition using a set concentration of the compound, usually 10 micromolar, on a scale from 0-10%, with 100% representing complete inhibition. (D.I. 153 at 29)

[35] IC_{50} is a measure of the biochemical function of a compound, indicating the quantity of the drug required to inhibit a biological process (or component of a process, *i.e.*, an enzyme, cell, cell receptor or microorganism) by half. *See gen.* www.wikipedia .org/wiki/IC50.

ii. Substructure searches

65. Glaxo distanced itself from Elgoyhen at trial, asserting that GR30040x was identified through a substructure search of GR35273, a beta-carboline compound having the following structure.[36]



66. Rafferty opined at trial that Labaudiniere identified GR35273, a compound of interest taken from Glaxo's "APOB100"[37] program, "another internal discovery program in Glaxo," in an effort to identify new leads for the PDE5 program. (D.I. 146 at 1202:5-18) GR35273 was tested on March 11 and 12, 1992, and was identified as an "impressive" PDE5 inhibitor. (*Id.*; DTX-1G at GLAX13202) According to Rafferty, Labaudiniere then undertook substructure searches based on the tetrahydro beta-carboline

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[36] Glaxo argues in its papers that "in May 1992, the Elgoyhen publication **reinforced** Dr. Labaudiniere's interest in beta-carbolines as potential PDE-5 inhibitors by showing that they could relax blood vessels." (D.I. 150 at 8) (emphasis added)

[37] APOB-100 is one of the two main isoforms of apolipoprotein B, the primary apolipoprotein of low-density lipoproteins ("LDL", commonly referred to as "bad cholesterol"). *See gen.* www.wikipedia.org/wiki/apolilipoprotein B.

fragment[38] of GR35273, leading to the identification of GR30040x (among other compounds), which was tested on April 23, 1992. (D.I. 146 at 1202:5-18, 1204:15-1206:14) Rafferty explained that, among the compounds tested by Glaxo between March and July 1992, there are "a rather disproportionate number of tetrahydro beta-carbolines, which suggests [ ] a search was conducted . . . and that Dr. Labaudiniere was exploring possibilities that turned up from that search." (*Id.* at 1299:1-5)

a. Documentary evidence

67. Minutes of a meeting held by Glaxo's Cardiovascular Research Management Committee on April 9, 1992 describe GR35273 as a compound synthesized by Prof. Campbell of Bath University that "selectively down-modulates apoB-100 production."[39] (JTX-22 at GLAX25738) Notes from that same committee's meeting on June 11, 1992 reflect that

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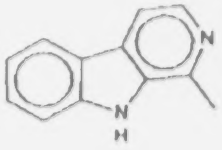
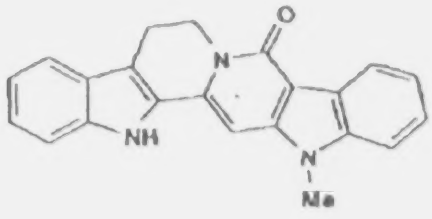
[38] Tetrahydro beta-carboline has the following structure.



[39] This mention of GR35273 occurred in the section entitled "Status Reports" and subtitled "6.1 Atherogenic and Thrombogenic Risk Factors." (JTX-22 at GLAX25738) Aside from an appendix containing its structure, the document does not appear to mention GR35273 elsewhere. (*Id.*)

> GR35273x, a compound coming from our APOB100 screen[,] displayed a high PDE V inhibition activity (IC50=30nm). A closed analogue AH20905xx displayed a similar activity (IC50=50nm). These compounds can be considered as conformationally constrained analogues of zaprinast, which are not patented as PDE V inhibitors. We are starting now a chemical programme on GR35273x analogues.

(JTX-24 at GLAX10365) Minutes from Glaxo's PDE Project meeting of June 23, 1992 (hereinafter, the "June 23, 1992 minutes") also list GR35273x as an analog of zaprinast, having the following structure[40]:



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[40] Plaintiff points to JTX-15 at GLAX16277-80, an untranslated version of minutes from an October 1992 Glaxo France strategy meeting, in support for the proposition that the PDE Project team "debated and concluded [in October 1992] that GR35273x was more appropriately considered a carboline than a zaprinast analog." (D.I. 154 at 10) No English translation appears to have been admitted and the court is not in the position to judge this statement. The court does note, however, that GR35273x appears to contain the beta-carboline core (three-ringed) structure.

(JTX-13 at GLAX16000) At this same meeting, GR30040x was characterized as a "new" PDE5 inhibitor.[41] (*Id.* at GLAX15986)

68. Also of record are the untranslated minutes of a PDE Meeting held at Glaxo France on September 9, 1992. (DTX-AQ) Among these minutes appears a "β-carbolines" chart, handwritten by Labaudiniere. (*Id.* at GLAX16099) GR30040 is structurally depicted among several compounds related to βCCE[42] (including a compound designated as GR142799); structure-activity relationships between the various compounds are noted. (*Id.*; D.I. 144 at 894:17-22)

69. Glaxo's "PDE V Inhibitors Project Annual Report for the Year Ending 30/4/03" (hereinafter, the "1992-93 Annual Report"), issued April 30, 1993,[43] discusses results of zaprinast analogues as well as "[a] new series of PDE V inhibitors . . . based on [a] tetrahydro-β-carboline structure," the best of which was identified as GF185990. (DTX-P, abstract) Additionally, the 1992-93 Annual Report states as follows:

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[41] Plaintiff does not point to an English translation of JTX-13. It is clear ,from the transcript that GR30040x was characterized as a "new" PDE5 inhibitor, though little else from this document is readily discernable. (D.I. 146 at 1250:1-15)

[42] The precise nature of the relationship (analogs, derivatives, etc.) is unclear.

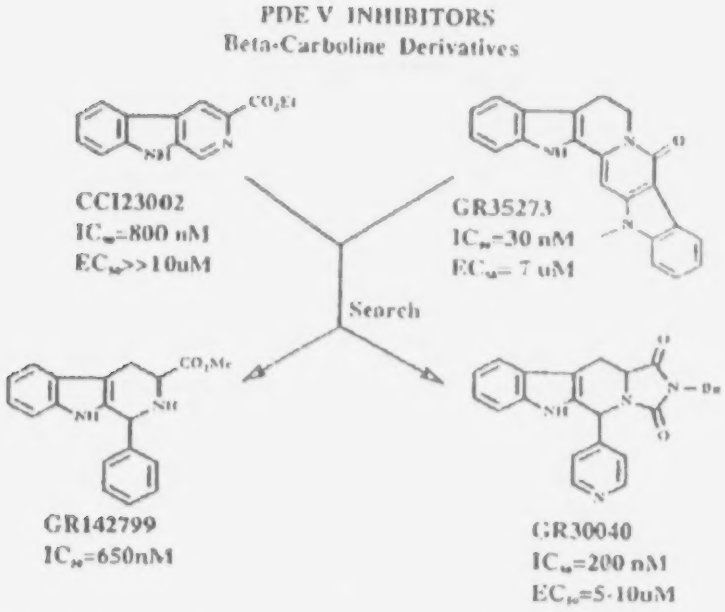
[43] The 1992-93 Annual Report is in memorandum format, addressed from Labaudiniere to Drs. Baxter, Finch, and Johnson of Glaxo France, with distribution to Glaxo's central files, 30 other employees (presumably scientists), and a department titled "Science Information, Les Ulis." (DTX-P)

4. 7. β-Carboline Series

4. 7. a- GR30040 analogues

It is a new series of compounds we began to study last year starting from literature data on β-carboline and benzodiazepine derivatives having some vasorelaxant effect on precontracted rat aortic rings. These compounds displayed in our hand some PDE V inhibition activities. Substructure searches from β-CCE and GR35273 on tetrahydro-β-carboline analogues in GLAX led to the identification of GR30040, a specific PDE V inhibitor, with activities similar to zaprinast (see figure 11). Studies have been performed to improve potency.

(DTX-P at 9) Figure 11, as referenced above, is reproduced below. Compound CC123002 is βCCE.



70. A 2003 Glaxo document also contains the same illustration (hereinafter, the "Beta-Carboline Derivatives Chart"). On February 24, 2003, Labaudiniere sent a report entitled "Progress in the Chemistry and Biology of PDE V Inhibitors" to Dr. Steve Stimpson at Glaxo.[44] (DTX-SU) This report identified three compounds, including βCCE, for "evaluation as PDE V inhibitors."[45] (*Id.* at GLAX16454) The Beta-Carboline Derivatives Chart was provided. (*Id.* at GLAX16455)

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[44] "Enclosed are the acetates of the last ICOS [meeting] for the overview presentation and the cellular biology working session where all the data relevant for PDE V inhibition were presented." (DTX-SU)

[45] Several tetrahydro-beta-carboline PDE5 inhibitors (GF169502; GF171885; GF173322; GF173321) were also identified. (DTX-SU at GLAX16456)

b. Testimony

71. Labaudiniere testified that the term "search" in the Beta-Carboline Derivatives Chart indicates that GR142799 and GR30040x were identified through a substructure search. (D.I. 141 at 441:7-25) Labaudiniere testified that he used Glaxo's ChemBase system to "identify analogues with the beta-carboline core structure." (*Id.* at 436:23-437:3, 437:21-25) Daugan corroborated this testimony. (D.I. 144 at 891:12-892:24)

72. Elgoyhen published prior to the June 1992 testing of βCCE. There was some debate at trial regarding whether a substructure search of βCCE would yield the compounds tested by Glaxo on April 23, 1992, including GR30040x (as indicated by the Beta Carboline Derivatives Chart). Rafferty testified that substructure searches based on the βCCE scaffold, removing the ethylcarboxylate ester from the six-membered notrogen-containing ring (and leaving open the possibility for either single or double bonds on that ring), would have retrieved GR148799 as a result. (D.I. 146 at 1271:21-1272:25; DTX-TC) Plaintiff emphasizes that a substructure search based on the complete βCCE molecule, without modification, would not have returned any of the compounds tested on April 23, 1992. (D.I. 153 at 38, n. 31; D.I. 146 at 1274:3-11)

b. Plaintiff's challenges to Glaxo's inventorship theory based on GR35273x

73. Plaintiff challenges Glaxo's position that GR30040x was gleaned from substructure searches on GR35273x (rather than from substructure searches

based on the Vanderbilt Structural Features contained in 8-(4-OH-PT)-IMBX) in several additional ways. First, plaintiff points out that the documents do not seem to connect GR30040x and GR35273x. (D.I. 153 at 39) GR30040x is not described as a GR35273x analog in the foregoing meeting notes and minutes. Analogs of GR30040x were listed in the June 23, 1992 minutes, but GR35273x was not among them. (*Id.* at GLAX15995-96) GR30040x was characterized as a "new" PDE5 inhibitor. (*Id.* at GLAX15986)

74. Plaintiff also argues that, while Glaxo's internal 1992-93 Annual Report specifically ties the identification of GR30040x to a substructure search on GR35273, Glaxo held out to the scientific community in the Tadalafil Paper that GR30040x was identified through substructure searching using "the β-carboline scaffold" based upon the disclosures of Koe and/or Elgoyhen. (JTX-29 at ICOS737)

75. Finally, plaintiff argues, without testimonial support, that a substructure search based on "the structural elements the Glaxo scientists found important in GR35273x would have identified only one compound among the April 23rd compounds other than GR35273x itself." (D.I. 153 at 39, n.33; D.I. 154 at 10[46])

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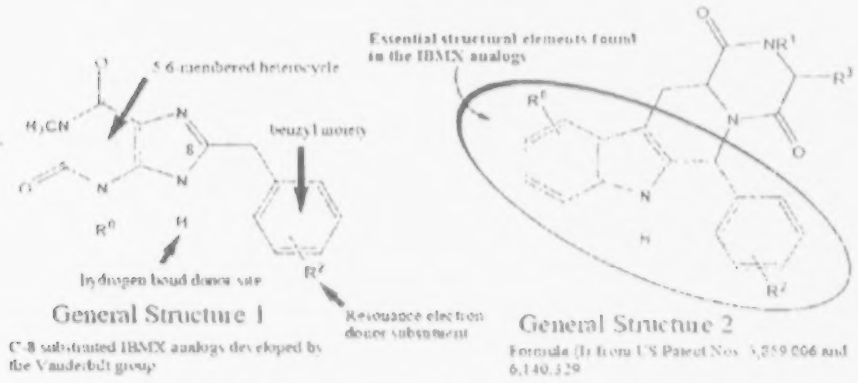
[46] The exhibits cited by plaintiff do not support this representation.

c. Plaintiff's theory that its disclosure of 8-(4-OH-PT)-IMBX led to the identification of GR30040x

76. Plaintiff asserts that 8-(4-OH-PT)-IMBX and the claimed compounds share a common scaffold. The portion of the compound of formula 1 corresponding to the asserted "Vanderbilt Structural Features" is circled below.

FIGURE 1



(D.I. 153 at 35)

77. As noted previously, the 1992 Research Proposal disclosed that some of the cGMP analogs plaintiff had created were not only PDE resistant, but acted like inhibitors of the enzyme by binding tightly to its catalytic site. (PTX-117 at VC250) Plaintiff asserts that the 1992 Research Proposal would have communicated to a chemist that the 8-position modification of the cGMP analogs prevented the cGMP from being degraded; attaching a "'biomimetic' of the ribose phosphate moiety, consisting of groups like 4-hydroxy phenylthio, to the 8-position of existing inhibitors, that biomimetic would bind in the same

region of the catalytic site as the ribose phosphate group that it is mimicking, and the result would be increased inhibition." (D.I. 153 at 23, citing D.I. 145 at 963:22-969:3)

78. Plaintiff asserts that Labaudiniere, upon receiving a copy of plaintiff's 1992 Research Proposal, conducted a substructure search based upon the Vanderbilt Structural Features contained in 8-(4-OH-PT)-IMBX. Plaintiff admits that no direct evidence supports its theory that such a search occurred.[47] Plaintiff relies on the following circumstantial evidence in order to demonstrate the likeliness of its hypothesis: (1) the 1992 Research Proposal contained impressive and stand-out results for 8-(4-OH-PT)-IMBX; (2) these results came from a respected source; (3) a substructure search based on the Vanderbilt Structural Features could have been performed with ease in only a few minutes; (4) On April 23, 1992, a few weeks after Labaudiniere received the 1992 Research Proposal, Glaxo tested 29 compounds for PDE5 inhibition including zaprinast; (5) none of these 29 compounds had originally been developed and registered in Glaxo France; and (6) each compound had a skeleton including a "6-membered ring fused to a 5-membered ring"; (7) 26 of the 29 compounds tested had "some substitution at the 8-position," as did the IMBX analogues identified by plaintiff in the 1992 Research Proposal; and (8) 11 of the 29 compounds contained both "a 6-member ring fused to a 5-member ring, with some substitution at

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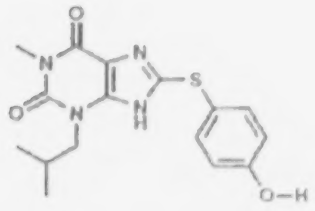
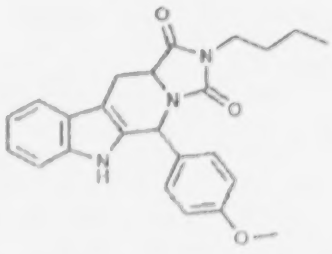
[47] (D.I. 154 at 4 ("Vanderbilt need not prove specifically how that occurred, but simply how it logically could have occurred."))

the 8-position" (*i.e.*, the so-called "Vanderbilt Structural Features"). (D.I. 153 at 26-28)

79. Upon Glaxo's identification of GR30040x, plaintiff asserts that Daugan incorporated into that compound "the only element of the Vanderbilt Structural Features and design that was lacking in GR30040x," electron-donating substituent on the phenyl ring. (D.I. 153 at 31) The result was GF173321x, having the following structure (as compared to 8-(4-OH-PT)-IMBX):



8-(4-Hydroxy phenylthio)-IBMX



GF 173321X

(*Id.*) According to plaintiff, Daugan and Labaudiniere "completely absorbed the Vanderbilt design and Vanderbilt Structural Features with the synthesis of GF173321 x."[48] (*Id.* at 34)

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[48] On or about November 23, 1992, another Glaxo chemist synthesized a zaprinast analog, GF178534x, incorporating the alleged "Vanderbilt Structural Features," which plaintiff asserts is "[f]urther evidence of Dr. Labaudiniere's role in directing the modifications made to GR30040x[.]" (D.I. 153 at 32)

To be clear, plaintiff does not assert in this litigation that Labaudiniere should be named as a co-inventor on either the '006 or '329 patents.

4. Modifications to GR30040x

80. According to plaintiff, the methoxy substituent, or the "electron-donating substituent on the phenyl ring," was "the only element of the Vanderbilt Structural Features and design that was lacking in GR30040x." (D.I. 153 at 31) Plaintiff asserts that the first modification made by Daugan to GR30040x was to replace the pyridine ring with a combination of a phenyl ring and an electron-donating methoxy substituent. (D.I. 153 at 30) Plaintiff asserts that these changes occurred simultaneously, "compel[ling] the conclusion that Dr. Labaudiniere directed Dr. Daugan to make them as a direct result of Dr. Labaudiniere's knowledge of the Vanderbilt design from the 1992 Research Proposal." (D.I. 154 at 14) In support for its assertion that both modifications occurred together, plaintiff cites to Daugan's testimony. (D.I. 153 at 30) Daugan, however, stated only that "[t]he first thing [he] did in this series was explore the replacement of the pyridinyl[ ] moiety with other heterocyclic or aromatic moieties." (896:2-4)

81. Plaintiff asserts that Daugan next continued to make "obvious" modifications to GF173321x, "the Vanderbilt Structural Features persist[ing] throughout," including "the replacement of the 5-member hydantoin ring with a 6-member piperazinedione ring," and eventually synthesized the first compound with all of the features of formula 1 of the '006 patent. (D.I. 153 at 34) In support, plaintiff relies upon the testimony of Labaudiniere. (*Id.*) Labaudiniere stated that modifying the phenyl ring at C5 would have been an obvious location to modify the GR30040x molecule. (D.I. 141 at 424:11:425:18) Labaudiniere also testified that there are a "standard

group of substitutions or additions" that would be tried with any molecules of interest, in a "trial-and-error" fashion. (*Id.* at 426:2-17) He stated that the "n-substitution on the hydantion ring," as discussed in the Tadalifil Paper, was an "obvious place to make a modification." (*Id.* at 426:18-24) Because the hydantion series of molecules had poor oral pharmokinetics, meaning that they were generally ineffective oral drugs, further modifications to the hydantion were made leading eventually to the 6-member piperazinedione ring. Labaudiniere characterized the 6-member piperazinedione ring as "a possibility among others." (*Id.* at 427:6-428:24) There was no specific motivation to move from a 6-member ring from the 5-membered ring, only to find an orally active compound. (*Id.*)

F. Discussion

82. As noted previously, 35 U.S.C. § 116 sets "no explicit lower limit on the quantum or quality of inventive contribution required for a person to qualify as a joint inventor." *Fina Oil*, 123 F.3d at 1473. Federal Circuit jurisprudence makes clear, however, that a person is a joint inventor "only if he contributes to the conception of the claimed invention." *Eli Lilly & Co. v. Aradigm Corp.*, 376 F.3d 1352, 1358-59 (Fed. Cir. 2006) (collecting cases). "The line between actual contributions to conception and the remaining, more prosaic contributions to the inventive process that do not render the contributor a co-inventor is sometimes a difficult one to draw." *Id.* at 1359.

83. The Federal Circuit has provided clear guidance in the context of claims to chemical compounds. "Conception of a chemical substance includes

knowledge of both the **specific chemical structure of the compound** and an operative method of making it," unless "a method of making a compound with conventional techniques is a matter of routine knowledge among those skilled in the art, [in which case] a compound has been deemed to have been conceived when it was described." *Burroughs Wellcome Co. v. Barr Labs., Inc.*, 40 F.3d 1223, 1230 (Fed. Cir. 1994) (emphasis added); *Oka v. Youssefyeh*, 849 F.2d 581, 583 (Fed. Cir. 1988). That is, "[c]onception does not occur unless one has a mental picture of the structure of the chemical, or is able to define it by its method of preparation, its physical or chemical properties, or whatever characteristics sufficiently distinguish it. It is not sufficient to define it solely by its biological activity[.]" *Amgen, Inc. v. Chugai Pharm. Co., Ltd.*, 927 F.2d 1200, 1206 (Fed. Cir. 1991).

84. Indeed, on facts analogous to those at bar,[49] the Federal Circuit in *The Board of Education of the Board of Trustees of Florida State University v. American Bioscience, Inc.*, 333 F.3d 1330 (Fed. Cir. 2003) (hereinafter, "*American Bioscience*"), declined to aid as inventors scientists who contributed the "starting materials" for a chemical compound. The Court there held that conception of a chemical compound requires "a conception of the specific compounds being claimed, with all of their component substituents." *Id.* at 1340. To put the point another way, "[h]aving in mind

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[49] The patent at issue in *American Bioscience* claimed three compounds which are analogs of docetaxel, an anticancer drug (similar to the natural compound paclitaxel) having two distinct substituents: (1) a 10-hydroxy group; and (2) a tertbutoxycarbonyl group attached to its 3' nitrogen atom. 333 F.3d at 1332-33. Scientists at Florida State University ("FSU"), including Robert Holton ("Holton") and Chunlin Tao ("Tao"), made paclitaxel analogs, including "PNIP," a promising anticancer compound having a 10-acetoxy group substituent. *Id.* at 1334. Following an industry conference at which Holton spoke regarding the synthesis of paclitaxel, scientists at VivoRx Pharmaceuticals, predecessor to American Bioscience, Inc., hired Tao and assigned him the task of creating docetaxel analogs using 10-deacetyl baccatin, a compound similar to that (baccatin III) used at FSU to synthesize paclitaxel but having a 10-hydroxy group. Tao made several compounds and a patent application was filed. Issuing were claims to three docetaxel analogs having the 10-hydroxy group. Because there was "no evidence of record that the idea of making [paclitaxel] analogs having a both a 10-hydroxy group (i.e., [docetaxels]) and a nitro functional group came from anyone other than [ABI's inventors]," or any "evidence of conception by Holton or anyone else at FSU of analogs having the combination of a 10 hydroxy group, a nitrophenyl group, and an N-alkoxy-carboyl (*i.e.*, tertbutoxycarbonyl, isopropoxycarbonyl, or isubutoxycarbonyl) substituent," FSU's arguments fell short of meeting the clear and convincing standard of proof required to prove inventorship. *Id.* at 1339, 1341.

specific portions of a claimed compound is not the same as conceiving the compound with all of its components." *Id.*

85. The same result is compelled in the case at bar. The "Vanderbilt Structural Features" constitute no more than a "specific portion[] of a claimed compound" in the language of *American Bioscience*. The record is devoid of evidence that Corbin, Francis, and/or Konjeti communicated to Glaxo a compound of the general structure of Formula 1 of the patents at issue. Plaintiff concedes that, prior to January 21, 1994 (the priority date for Glaxo's U.K. application), its scientists were not aware of the existence of (or structure of) any of the claimed compounds. (DTX-RG at Response Nos. 13-22) There is no indication that Corbin, Francis, and Konjeti were working with beta-carbolines.

86. Because there is no evidence that Corbin, Francis and Konjeti ever conceived the "specific chemical structure of the compound" claimed, *Burroughs Wellcome*, 40 F.3d at 1230, or "the compound with all of its components," *American Bioscience*, 333 F.3d at 1340, or communicated that compound to Glaxo,[50] plaintiff has failed to

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[50] Defendant points out that plaintiff admitted that Corbin, Francis and Konjeti never had any direct communication with Daugan regarding this subject matter. (DTX-RG at Response Nos. 23-26) Plaintiff seeks an inference that Labaudiniere communicated the "Vanderbilt Structural Features" to Daugan, and directed Daugan to incorporate them into his research. Notwithstanding the lack of evidence in this regard, even had Corbin, Francis or Konjeti communicated 8-(4-OH-PT)-IMBX to Daqgan directly, plaintiff could not demonstrate on this record

demonstrate, by clear and convincing evidence, that Corbin, Francis and Konjeti are coinventors of the patents at issue.

87. This is not to say that Corbin, Francis and Konjeti did not make contributions to Daugan's inventive process; only that, under the applicable law, these contributions fall more into the category of "prosaic" contributions because they did not conceive the invention as claimed. *Eli Lilly*, 376 F.3d at 1358-59.

88. Notwithstanding the result compelled by Federal Circuit precedent in this case, the court notes that it finds defendant's litigation position troubling. Defendant submits that Glaxo made no use of plaintiff's disclosure that 8-(4-OH-PT)-IMBX was "160-fold more potent that the parent IMBX and 6-fold more potent than the best existing inhibitor, zaprinast" – a position that this court deems untenable. (D.I. 150 at 3 ("[Plaintiff] did not provide any direct (or even circumstantial) evidence that . . . the four "Structural Features" played **any** role in Dr. Daugan's conceptions.") (emphasis in original))

89. By the spring of 1992, of the twenty original Glaxo Cardiovascular Discovery grants, only one remained – and plaintiff was its recipient. (PTX-121) It is difficult to imagine that Glaxo maintained this particular relationship for no particular benefit. Defendant loses credibility in the court's view for failing to acknowledge that Glaxo made any use of

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that Corbin, Francis or Konjeti ever conceived a compound within the family of claimed compounds.

plaintiff's disclosure. There was a consensus among the witnesses at trial that the 160-fold result would have commanded attention. (D.I. 145 at 1067:9-20 (acknowledging result was "interesting"); D.I. 146 at 1233:1-4 (acknowledging that result was "significant," despite denying that a single test result would have been "particularly useful") (Rafferty))

90. Defendant's position is also untenable in view of the fact that, although they are (in whole) different molecules having different properties, 8-(4-OH-PT)-IMBX, GR30040x, GF173321x, and the claimed compounds share a common scaffold having a common shape (three-dimensional configuration). It is the court's understanding that the shape of an inhibitor is directly related to its ability to bind to the enzyme. Corbin communicated to Glaxo on several occasions the importance of the spacial relationships of the substituents he was investigating: for example, Corbin's April 1991 minuscript, discussing the 8-position substituent (*supra* no. 29), and the 1992 Research Proposal, discussing the affinity of the 1,2 and 8-position modifications (*supra* nos. 51, 77).

91. Further, there is a close proximity in time of the relevant events which renders plausible plaintiff's theory that Glaxo did take note of 8-(4-OH-PT)-IMBX and incorporated the "Vanderbilt Structural Features" into the beta-carboline research it was conducting.[51]

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[51] To summarize, the 1992 Research Proposal was dated February 24, 1992. GR35273X was first tested with PDE5 at Glaxo France on March 11 and 12, 1992. Labaudiniere was sent a copy of the 1992 Research Proposal on April 8, 1992. A 10 micromolar concentration test was performed on GR30040x on April 23, 1992, followed by PDE5 inhibition testing on April 24, 1992. Further

The court notes that nowhere in its papers did defendant articulate why Labaudiniere selected tetrahydro beta-carbolines (more specifically, the tetrahydro beta-carboline fragment of GR35273) for his substructure searches.[52] (*See supra* no. 66) Notwithstanding, the court views plaintiff's theory (which is devoid of evidence regarding the alleged substructure searches based on 8-(4-OH-PT)-IMBX) and defendant's story (which is devoid of the aforementioned foundation) equally plausible with respect to the identification of GR30040x.[53]

92. Ultimately, even if the court were to find that plaintiff's disclosure of 8-(4-OH-PT)-IMBX led to the identification of GR30040x and the subsequent discovery of tadalafil, *American Bioscience* precludes the result plaintiff seeks: namely, that the contribution of a molecular scaffold in the context of one molecule (here, 8-(4-OH-PT)-IMBX) renders the disclosing party or parties inventors of a different family of molecules containing the same scaffold (here, the compounds of Formula I, including tadalafil). The chemical arts have frequently been characterized by the courts as "unpredictable." Minor modifications to a compound may drastically alter its properties and effectiveness;

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testing of GR30040x occurred alongside 26 other compounds on June 17, 1992. GR30040x was identified as a "new" PDE5 inhibitor during the June 23, 1992 meeting.

[52] Glaxo's 1992-93 Annual Report states only that the literature suggested the use of beta-carbolines generally. (DTX-P at 9)

[53] Notably, even if GR30040x were the invention, the balance would not so tip in favor of plaintiff such as to constitute clear and convincing evidence.

when isolated, particular portions of a molecule are likely to exhibit different chemical properties. For these reasons, the Federal Circuit has indicated that inventorship must be measured in terms of the complete chemical structure claimed as compared to its functional components, just as the validity and the scope of claims to chemical compounds are measured in terms of the complete chemical structure (and very close structural equivalents).[54] The court declines to expand the reach of 35 U.S.C. § 116 in the manner espoused by plaintiff.

III. CONCLUSION

93. For the reasons discussed above, the court concludes that plaintiff has failed to prove, by clear and convincing evidence, that Corbin, Francis, or Konjeti are inventors of the '006 or '329 patents. Therefore, judgment shall be entered in favor of defendant and against plaintiff. An appropriate order shall issue.

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[54] *See, e.g., PPG Indus., Inc. v. Guardian Indus. Corp.*, 75 F.3d 1558, 1564 (Fed. Cir. 1996) ("In unpredictable art areas, this court has refused to find broad generic claims enabled by specifications that demonstrate the enablement of only one or a few embodiments and do not demonstrate with reasonable specificity how to make and use other potential embodiments across the full scope of the claim."); *Bilstad v. Wakalopulos*, 386 F.3d 1116, 1125 (Fed. Cir. 2004) ("[I]f the art is unpredictable, then disclosure of more species is necessary to adequately show possession of the entire genus") (citations omitted); *see also In re Jones*, 958 F.2d 347, 350 (Fed. Cir. 1992) (noting that "particular types or categories of structural similarity without more" may give rise to prima facie obviousness, but "generalization is to be avoided insofar as specific structures are alleged to be prima facie obvious one from the other").

APPENDIX C

IN THE UNITED STATES DISTRICT COURT FOR THE DISTRICT OF DELAWARE

Civ. No. 05-506-SLR

[Filed January 29, 2009]

VANDERBILT UNIVERSITY,	)
	)
Plaintiff,	)
	)
v.	)
	)
ICOS CORPORATION,	)
	)
Defendant.	)
	)

JUDGMENT IN A CIVIL CASE

For reasons stated in the court's memorandum opinion and order of January 27, 2009;

IT IS ORDERED AND ADJUDGED that judgment be and is hereby entered in favor of defendant Icos Corporation and against plaintiff Vanderbilt University.

/s/ Sue L. Robinson
United States District Judge

Date: 1/29/09

/s/ Nicole Fasarro
(By) Deputy Clerk

APPENDIX D

NOTE: This order is nonprecedential.

UNITED STATES COURT OF APPEALS FOR THE FEDERAL CIRCUIT

No. 2009-1258

[Filed June 23, 2010]

VANDERBILT UNIVERSITY,	)
	)
Plaintiff-Appellant,	)
	)
v.	)
	)
ICOS CORPORATION,	)
	)
Defendant-Appellee.	)
	)

Appeal from the United States District Court for the District of Delaware in case no. 05-CV-506, Judge Sue L. Robinson.

ORDER

A combined petition for panel rehearing and for rehearing en banc having been filed by the Appellant, and a response thereto having been invited by the court and filed by the Appellee, and the petition for rehearing and response, having been referred to the

panel that heard the appeal, and thereafter the petition for rehearing en banc and response having been referred to the circuit judges who are in regular active service,*

UPON CONSIDERATION THEREOF, it is

ORDERED that the petition for panel rehearing be, and the same hereby is, DENIED and it is further

ORDERED that the petition for rehearing en banc be, and the same hereby is, DENIED.

The mandate of the court will issue on June 30, 2010.

Circuit Judge Lourie did not participate in the vote.

FOR THE COURT,

/s/ Jan Horbaly [LB]
Jan Horbaly
Clerk

Dated: 06/23/2010

cc: Robert S. Brennen
Kevin M. Flowers

VANDERBILT UNIV V ICOS CORP, 2009-1258
(DCT - 05-CV-506)

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* Paul R Michel, who retired as Chief Judge on May 31, 2010, did not participate in the decision on rehearing en banc.

Supreme Court, U.S.
FILED
DEC 20 2010
OFFICE OF THE CLERK

No. 10-412

IN THE

Supreme Court of the United States

VANDERBILT UNIVERSITY,

Petitioner,

v.

ICOS CORPORATION,

Respondent.

ON PETITION FOR A WRIT OF CERTIORARI TO THE UNITED STATES COURT OF APPEALS FOR THE FEDERAL CIRCUIT

BRIEF IN OPPOSITION

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QUESTIONS PRESENTED

1. Whether the lower courts were correct in rejecting Petitioner's request to add its scientists as co-inventors on patents under 35 U.S.C. § 256, where the district court found that Petitioner's theory regarding its scientists' alleged contribution to the inventions, when compared to the contrary account established by the patent owner, was at best only "equally plausible."

2. Whether a court of appeals may affirm a district court's judgment on an alternative ground supported by the record.

CORPORATE DISCLOSURE STATEMENT

ICOS Corporation is a wholly-owned subsidiary of Eli Lilly & Company, which is publicly traded.

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IN THE

Supreme Court of the United States

No. 10-412

VANDERBILT UNIVERSITY,

Petitioner,

v.

ICOS CORPORATION,

Respondent.

ON PETITION FOR A WRIT OF CERTIORARI TO THE UNITED STATES COURT OF APPEALS FOR THE FEDERAL CIRCUIT

BRIEF IN OPPOSITION

INTRODUCTION

Neither of the questions presented by Petitioner Vanderbilt University merits this Court's attention. Vanderbilt lost this case not because it faced a "clear and convincing" standard of proof, but because it failed to convince the district court that its theory based on speculation was any more than "equally plausible" when compared to ICOS's contrary account based on evidence. Pet. App. 82a. There is no need for this Court to review a case where, as here, the question presented will have no effect on the outcome. Vanderbilt's petition should be denied.

1. Although the question this Court will review in *Microsoft Corp.* v. *i4i Ltd. Partnership* (No. 10-290)—the appropriate standard of proof for claims of patent invalidity over prior art references not submitted to the Patent Office—bears some resemblance to Vanderbilt's first question presented, this Court's review of *i4i* does not warrant granting or even holding Vanderbilt's petition, for at least two reasons.

First, and critically, the Federal Circuit's disposition of this case was manifestly correct *regardless* of what standard of proof is applied. As the district court found, and Vanderbilt does not deny, the record contains a complete "lack of evidence" supporting Vanderbilt's argument on several essential points. Pet. App. 79a-80a n.50. The district court accordingly held that, at the very most, Vanderbilt's speculative theory of events was "equally plausible" when compared to ICOS's contrary account based on the evidence. *Id.* 82a. That finding is dispositive, because it confirms that Vanderbilt failed to prove *even by a preponderance of the evidence* that its scientists should be added as co-inventors. Where, as here, the resolution of the question presented "is irrelevant to the ultimate outcome of the case before the Court, certiorari may be denied." Gressman *et al.*, *Supreme Court Practice* § 4.4(f), at 248 (9th ed. 2007).

Second, even were this Court to conclude in *i4i* that a preponderance-of-the-evidence standard applies to invalidity challenges based on prior art references not submitted to the Patent Office, that would not compel application of a similar standard in the correction-of-inventorship context of this case. Judicial decisions requiring clear and convincing evidence in order to correct inventorship date back decades, including prior to the 1952 enactment of the current Patent Act. Con-

gress's enactment of 35 U.S.C. § 256 did not purport to alter that common law standard, and Congress's continued failure to disturb it demonstrates legislative acquiescence. *See, e.g.*, *Merck & Co.* v. *Reynolds*, 130 S. Ct. 1784, 1795 (2010) ("We normally assume that, when Congress enacts statutes, it is aware of relevant judicial precedent."); *Watson* v. *United States*, 552 U.S. 74, 82-83 (2007) (prolonged congressional inaction following judicial construction of a statute "'enhance[s] even the usual precedential force'" accorded statutory interpretations (quoting *Shepard* v. *United States*, 544 U.S. 13, 23 (2005))). Congress's approval of the clear-and-convincing-evidence standard is confirmed by its continued refusal to revise the proof requirements in correction-of-inventorship cases. Notably, not one of the amici supporting Microsoft's petition in *i4i* has supported Vanderbilt's petition here.

2. Vanderbilt's second question presented is also unworthy of review. It is settled law that "[a] successful party in the District Court may sustain its judgment on any ground that finds support in the record." *Jaffke* v. *Dunham*, 352 U.S. 280, 281 (1957) (per curiam). Every court of appeals has applied this rule repeatedly, including in cases in which the district court has committed harmless legal error. Nothing in this Court's decision in *Pullman-Standard* v. *Swint*, 456 U.S. 273 (1982), alters that established principle of appellate review, particularly where—as here—the court of appeals affirms on a basis that the district court itself adopted as an alternative ruling.

STATEMENT

A. Dr. Daugan's Invention Of The Patented Compounds

This case turns on research conducted by Dr. Alain Daugan, a medicinal chemist at a Glaxo Wellcome Inc. research facility in Les Ulis, France. Pet. App. 33a-36a. In the early 1990s, Dr. Daugan invented certain chemical compounds that, along with compositions comprising them and methods for using them, are claimed in U.S. Patents Nos. 5,859,006 (the '006 patent) and 6,140,329 (the '329 patent), both of which were assigned to Respondent ICOS Corporation. The parties "agree that Dr. Daugan was the first to conceive" the claimed compounds. *Id.* 23a.

The specific compounds Dr. Daugan invented provide for increased relaxation of smooth muscle tissue, resulting in the widening of blood vessels (vasodilation) and increased blood flow. Pet. App. 34a. The compounds, known as "PDE5 inhibitors," inhibit the function of an enzyme called phosphodiesterase V ("PDE5"), which would otherwise break down a cyclic nucleotide called cyclic guanosine monophosphate ("cGMP"). When not broken down, cGMP activates another protein called cGMP kinase, which causes smooth muscle tissue to relax. *Id.*

The net effect of PDE5 inhibitors is smooth-muscle relaxation and increased blood flow. Pet. App. 34a. As a result, PDE5 inhibitors can be effective in treating erectile dysfunction ("ED"). *Id.* 3a. One of the compounds Dr. Daugan invented, tadalafil, became the active ingredient in Cialis®, one of the world's best-selling drugs for the treatment of ED.

Tadalafil and the other claimed compounds that Dr. Daugan invented are tetracyclic (*i.e.*, four-ringed)

molecules that comprise a particular three-ringed substructure known as a "beta-carboline." Pet. App. 59a. Dr. Daugan's invention of tadalafil resulted from a comprehensive chemical study between 1992 and 1994 that began with a "lead" compound that Glaxo designated GR30040x, which also had a beta-carboline substructure. *Id.* 60a. Dr. Richard Labaudinière, the head of chemistry and leader of Glaxo's PDE5 project in France, asked Dr. Daugan to modify GR30040x, which (along with other beta-carboline lead compounds) had been identified at Glaxo as a potent PDE5 inhibitor. *Id.* 62a. Dr. Daugan then worked independently to make structural modifications to the beta-carboline backbone (the "scaffold") of GR30040x.

Dr. Daugan conducted an extensive series of experiments as he sought, through "trial and error," to create a more potent, selective, and orally effective PDE5 inhibitor. Ct. App. J.A. 453:19-455:17. As part of that search, he made a series of analogs of GR30040x, creating "several hundred[]" compounds as he strove "to identify the best compound." *Id.* 674:12-20. For example, from June to December 1992, Dr. Daugan focused on compounds with a four-ring backbone comprising a three-ring beta-carboline structure linked to a five-membered "hydantoin" ring, but these proved ineffective when taken orally. *Id.* 693:23-700:3. Dr. Daugan then tried replacing the five-membered hydantoin ring found in the GR30040x analogs with a six-membered piperazinedione ring, a substitution that led to his discovery of a group of compounds that he later designated "Formula (I)" in the patents-in-suit. *Id.* 699:22-701:19, 2650, 7553-7562, 7517. Dr. Daugan continued studying and altering this new family of compounds, creating and testing scores of compounds with dispa-

rate chemical substituents, and by June 1993, he had invented tadalafil. *Id.* 662:6-664:4, 701:7-703:22.

Dr. Labaudinière explained his initial identification of GR30040x as a "lead" compound, testifying without contradiction that his attention was drawn to two other beta-carbolines, designated CCI23002 and GR35273, because scientific literature and a separate Glaxo project had described them as inhibiting PDE5. Ct. App. J.A. 470:7-471:4. Dr. Labaudinière searched Glaxo's chemical-compound database for compounds with similar substructures and discovered potential candidates for further research, including GR30040x. *Id.* 470:7-25, 967. This unchallenged account was confirmed by testimony from Dr. Daugan and two experts, as well as by minutes from Glaxo meetings and Glaxo France's contemporaneous 1992-1993 Annual Report. Pet. App. 65a-69a; Ct. App. J.A. 2639-2699.

Dr. Daugan and Glaxo first sought patent protection for tadalafil and the other claimed compounds in 1994, when Glaxo filed a U.K. patent application. A U.S. patent application was filed under the Patent Cooperation Treaty in 1995, issuing as the '006 patent in 1999. A second U.S. patent application directed specifically to the use of tadalafil to treat ED was filed in 1996 and issued as the '329 patent in 2000. The relevant patent claims are directed to particular chemical compounds, pharmaceutical compositions comprising those compounds, and methods for using those compounds. Pet. App. 34a-36a. The rights in these inventions had previously been assigned to ICOS. *Id.* 7a, 34a.

In 2002, ICOS obtained approval to market tadalafil as the active ingredient in Cialis®, a commercial ED drug. In 2007, ICOS was acquired by Eli Lilly & Company.

B. Proceedings in the District Court

On July 20, 2005, years after Dr. Daugan obtained his patents and well after Cialis® became a commercial success, Petitioner Vanderbilt University sued ICOS under 35 U.S.C. § 256, alleging that three of its professors—Dr. Jackie D. Corbin, Dr. Sharron H. Francis, and Dr. Sekhar R. Konjeti—should be added to the patents-in-suit as joint inventors with Dr. Daugan. Pet. App. 2a.

The district court held a bench trial on Vanderbilt's correction-of-inventorship claim. Vanderbilt did not contend that its professors had conceived tadalafil; the parties agreed that Dr. Daugan alone had done so. Pet. App. 23a. The Vanderbilt professors acknowledged that they had never had any contact with Dr. Daugan: Dr. Corbin admitted that he "never met Dr. Daugan," had no "direct connection with Dr. Daugan," had "never worked together with Dr. Daugan to solve any kind of a problem," and was "working independently" from Dr. Daugan. Ct. App. J.A. 386:4-387:5. Dr. Konjeti similarly admitted that he "didn't know that Dr. Daugan existed" and "never had any collaboration" with him. *Id.* 595:16-23. The record contains no evidence or suggestion that either the professors or Vanderbilt ever filed any application claiming inventorship of any compounds comprising a beta-carboline substructure, and certainly not tadalafil or any of the other compounds claimed in the '006 patent.

The evidence also showed that the Vanderbilt professors had no inkling that the beta-carboline compounds Dr. Daugan was studying could even be used as PDE5 inhibitors. Pet. App. 79a (citing Vanderbilt's written responses to ICOS's Requests for Admission). Dr. Corbin admitted that he "didn't know that anyone

in the world was working on beta-carboline compounds to make PDE-5 inhibitors" in 1992 or 1993, and he "didn't think of using beta-carboline compounds" at that time. Ct. App. J.A. 383:3-14. Dr. Konjeti similarly admitted that he "didn't know that beta-carboline compounds could inhibit PDE," was not aware of the structure of the compounds claimed in the patents, and "hadn't thought of any methods for making the ... compounds claimed in the patents." *Id.* 592:5-593:20, 594:16-595:2. Accordingly, Vanderbilt likewise filed no patent applications directed to the uses of such compounds claimed in the '329 patent.

Instead of allegations as to conception of the compounds and uses at issue, Vanderbilt rested its claim to joint inventorship on a highly attenuated "theory" or "hypothesis." Pet. App. 72a, 73a, 82a. Specifically, Vanderbilt ventured that a *non-beta-carboline* PDE5 inhibitor its professors identified—a compound known as 8-(4-hydroxy phenylthio)-isobutylmethylxanthine, designated an "IBMX analog"—led to Dr. Daugan's invention of the beta-carboline compounds claimed in the patents. *Id.* 36a. Vanderbilt's theory involved a complex chain of hypothetical events, none of which was supported by evidence. Indeed, Vanderbilt admitted that it had "no direct evidence to support its view of the facts," but took the position that it "'need not prove specifically how [its version of events] occurred, but simply how it logically could have occurred.'" Pet. App. 17a; *see also id.* 73a.

Vanderbilt's theory was that Dr. Daugan's discovery of tadalafil resulted from the Vanderbilt professors' recognition of potent PDE5 inhibition by the IBMX analog (which was *not* a beta-carboline). The professors had included their finding regarding the IBMX analog in a January 3, 1992 research funding proposal

sent to Dr. Barry Ross, a scientist at Glaxo U.K. Pet. App. 5a. On April 8, 1992, Dr. Ross forwarded the proposal to a group including Dr. Labaudinière. *Id.* 6a. At that point, Vanderbilt's theory departed the realm of evidence and rested entirely on speculation. Vanderbilt contended, without evidentiary support, that (1) Dr. Labaudinière immediately read the proposal; (2) he somehow recognized four unidentified "structural features" of Vanderbilt's IBMX analog that were purportedly central to its inhibition of PDE5; and (3) he used some of those "features" to inform the database search that led him to identify GR30040x, which he then directed Dr. Daugan to research. *Id.* 73a-75a. Alternatively, Vanderbilt argued (4) that Dr. Daugan himself learned of the Vanderbilt professors' disclosure of the IBMX analog, and (5) used some of that IBMX analog's features to guide his modification of GR30040x, which eventually led to his invention of the patented compounds. *Id.* 75a-76a.

As mentioned, Vanderbilt had *no* direct evidence for its speculative chain of events. Indeed, the features that it argued Dr. Labaudinière utilized and conveyed to Dr. Daugan—which it now refers to as "Vanderbilt Structural Features"—were not identified as being necessary or sufficient for improving the potency of any PDE5 inhibitor in any contemporaneous document, including the January 1992 proposal or any other internal Vanderbilt documents. Ct. App. J.A. 423:11-425:3, 756:5-12, 763:13-765:19, 843:14-847:3, 1831-1836. Indeed, prior to an expert report and testimony in this case (*id.* 418:6-24), Vanderbilt had never referred to these elements as a related set of features in any communication to Glaxo. Nor did Vanderbilt name these elements the "Vanderbilt Structural Features" until after the trial had finished—the first such mention appeared in Van-

derbilt's post-trial brief. Dkt. No. 149 at 22 (D. Del. Feb. 25, 2008).

ICOS countered Vanderbilt's speculation with extensive evidence, including contemporaneous documents and undisputed testimony from fact and expert witnesses, all of which showed that the Vanderbilt professors' research had no influence on either Dr. Labaudinière or Dr. Daugan. As for Vanderbilt's first theory, unrebutted testimony showed that Dr. Labaudinière (1) did not conduct his search for beta-carboline compounds based on the supposed "Vanderbilt Structural Features"; (2) would not have conducted such a search because it would have been scientifically unsound and impractical; and (3) would not have discovered GR30040x by performing the search as Vanderbilt conjectured. Ct. App. J.A. 438:21-439:12, 470:7-471:4, 942:16-24. Indeed, Dr. Labaudinière's unrebutted testimony showed that he did not know about Vanderbilt's research until June 1993—months after Dr. Daugan conceived the claimed compounds. *Id.* 438:21-439:12, 7369.

Regarding Vanderbilt's alternative theory that Dr. Daugan himself knew of and was influenced by the Vanderbilt professors' IBMX analog, Dr. Daugan provided direct and unchallenged testimony that, before the lawsuit, he had never (1) seen any document written by the Vanderbilt professors, (2) seen the results of any experiment they conducted, (3) discussed their work with anyone, (4) known anything about their research, or (5) been influenced by any theory based on the "structural features" of an IBMX analog. Ct. App. J.A. 668:17-669:4. Rather, Dr. Daugan explained that his effort was an independent, extensive empirical research study based on trial and error, explicitly stating that "no information and no one influenced [him] in the

design and conception of the [claimed] compounds." *Id.* 674:6-7; *see also id.* 658:17-659:3, 660:5-9, 660:22-661:21, 674:3-20, 677:13-684:6, 693:19-703:17. Finally, Dr. Daugan testified that, even if he had known that the IBMX analog was a potent PDE5 inhibitor, that would not have helped him design the claimed beta-carboline compounds, because the two different kinds of compounds had no relevant structural similarity. *Id.* 673:1-11; *see also id.* 7516-7542.

The district court ruled that Vanderbilt failed to prove that Drs. Corbin, Francis, or Konjeti were inventors of either the '006 or '329 patents. Pet. App. 31a-83a. The court articulated two reasons for rejecting Vanderbilt's correction-of-inventorship claim. *First*, the court ruled that there was "no evidence that [the Vanderbilt professors] ever conceived the 'specific chemical structure of the compound' claimed," a matter the court deemed dispositive under binding precedent. *Id.* 79a-80a n.50. *Second*, the court noted the "lack of evidence" supporting Vanderbilt's theory that Dr. Labaudinière communicated any of Vanderbilt's "structural features" to Dr. Daugan. *Id.* 79a n.50. As for how Dr. Labaudinière identified GR30040x, while the court criticized ICOS's position in some respects (*id.* 80a-81a), its ultimate conclusion was that both parties' accounts were "equally plausible with respect to the identification of GR30040x." *Id.* 82a.

C. Proceedings in the Court of Appeals

The Federal Circuit affirmed on the second basis articulated by the district court. As to the first basis, the court of appeals accepted Vanderbilt's argument that a co-inventor need not have "an independent mental picture of the complete compound claimed"; it sufficed that "a group of co-inventors must collaborate and

work together to collectively have a definite and permanent idea of the complete invention." Pet. App. 22a.

However, the court of appeals affirmed based on the district court's finding that the parties' accounts of the identification of the GR30040x compound—which, though not claimed in the patents, was the linchpin of Vanderbilt's theory of co-inventorship—were "'equally plausible'" and that "Vanderbilt failed to produce any evidence of joint invention of tadalafil." Pet. App. 23a. Accordingly, the court ruled that, "under the correct legal test, Vanderbilt did not carry its burden. Thus, any erroneous interpretations of our case law were harmless error." *Id.*; *see also id.* 19a ("These errors, however, do not affect the outcome of this appeal and are therefore harmless in context. When tested by the correct law, the facts of the case still require affirmance.").

Judge Dyk concurred in part and dissented in part. Judge Dyk agreed that the evidence supported the district court's ruling that Dr. Daugan "did not himself directly utilize the Vanderbilt scientists' contributions." Pet. App. 26a. Judge Dyk maintained, however, that the court "could not have properly found that the Vanderbilt scientists made a contribution to the identification of GR30040x if it were 'equally plausible' that they did not make a contribution." *Id.* 28a. Alternatively, Judge Dyk believed that the district court's opinion could be read as irretrievably "tainted" by its legal error that a joint inventor was required to conceive the entire claimed invention. *Id.* 28a-29a.

The Federal Circuit denied Vanderbilt's petition for rehearing and rehearing en banc. Pet. App. 86a-87a.

REASONS FOR DENYING THE PETITION

I. THE STANDARD OF PROOF IS NOT OUTCOME-DETERMINATIVE AND DOES NOT MERIT REVIEW

Vanderbilt's attempt to hitch its wagon to this Court's grant of certiorari in *i4i* depends on ignoring Vanderbilt's failure to convince either the district court or the court of appeals that its theory of events based on speculation was any more plausible than ICOS's account of the invention based on evidence. Even if this Court were to grant certiorari, receive merits briefs, hear oral argument, and reverse the Federal Circuit's application of a "clear and convincing" standard of proof, the outcome would be exactly the same: a judgment that Vanderbilt failed to carry its burden, because the district court found that Vanderbilt's theory was no more than "equally plausible" compared to ICOS's account. Pet. App. 82a. The Court is rightly disinclined to review cases in which reversal will not affect the actual controversy between the parties, and it should not make an exception here.

Additionally, the Federal Circuit's settled requirement that a putative co-inventor must adduce clear and convincing evidence of inventorship in order to prevail under 35 U.S.C. § 256 is correct. The statute simply codified preexisting common law on the matter, which Congress has never abrogated. Regardless of the outcome in *i4i*, there is no reason to reconsider the standard of proof in correction-of-inventorship cases—an issue on which the Court has previously denied certiorari.

A. This Case Is An Unsuitable Vehicle Because Reversal On The Question Presented Cannot Alter The Outcome

Although the clear-and-convincing-evidence standard was invoked below to reinforce Vanderbilt's failure to support its theory with evidence, the courts below could and—based on their express statements—would have reached the very same result under a preponderance standard. As the district court and the court of appeals majority recognized, Vanderbilt's theory was at most "equally plausible" when compared to the account ICOS supported with evidence. Pet. App. 23a, 82a. It is settled—and Vanderbilt does not dispute—that "when the evidence is evenly balanced, the [burdened party] must lose." *Director, Office of Workers' Compensation Programs* v. *Greenwich Collieries*, 512 U.S. 267, 281 (1994); *see also Gonzales* v. *O Centro Espirita Beneficente Uniao do Vegetal*, 546 U.S. 418, 428 (2006) (government failed to carry its burden where the evidence was "in equipoise"); *Concrete Pipe & Prods. of Cal., Inc.* v. *Construction Laborers Pension Trust for S. Cal.*, 508 U.S. 602, 622 (1993) (preponderance-of-the-evidence standard requires "the trier of fact to believe that the existence of a fact is *more probable* than its nonexistence before [it] may find in favor of the party who has the burden" (emphasis added; internal quotation marks omitted)).[1]

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[1] Vanderbilt does not dispute the proposition that, even under a preponderance standard, it would still bear the burden of proof as the party seeking to change the status quo. *See, e.g.*, *Schaffer ex rel. Schaffer* v. *Weast*, 546 U.S. 49, 57-58 (2005) ("Absent some reason to believe that Congress intended otherwise, ... the burden of persuasion lies where it usually falls, upon the party seeking relief."); 1 Mueller & Kirkpatrick, *Federal Evidence* § 3.1, at 104

This Court generally does not grant certiorari to resolve legal issues that will not affect the outcome of the case in which they arise. *See, e.g.*, Gressman *et al.*, *Supreme Court Practice* § 4.4(f), at 248 (9th ed. 2007) (citing *Sommerville* v. *United States*, 376 U.S. 909 (1964)).[2] That practice is sound, as the fact that the decision below ultimately did not turn on the issue presented raises the question whether the issue is dispositive in *any* case, or at least arises sufficiently frequently to merit this Court's intervention.

Although Vanderbilt cites the number of amicus briefs supporting the petition in *i4i* (Supp. Br. 2), it is notable that *not one* amicus supported Vanderbilt's petition here, nor did any of the *i4i* briefs suggest that the Court should alter the longstanding requirement of clear and convincing evidence in correction-of-inventorship cases. Indeed, a Section 256 plaintiff must *corroborate* his or her own testimony with objective evidence—a common-law requirement of proof that Vanderbilt accepts as proper under the statute, while recognizing that it is "unique[]" to the correction-of-inventorship context. Pet. 20. Yet the independent corroboration requirement in correction-of-inventorship cases is closely linked to the requirement

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(3d ed. 2007) ("Perhaps the broadest and most accepted idea is that the person who seeks court action should justify the request, which means that the plaintiffs bear the burdens on the elements in their claims.").

[2] In *Sommerville*, the circuit panel was divided as to whether liability was governed by state or federal law, and the courts of appeals were similarly divided, but the disagreement was theoretical because the defendant would have been liable under either approach. *United States* v. *Sommerville*, 324 F.2d 712, 714, 717 n.16 (3d Cir. 1963); *see also id.* at 720 (Steel, J., concurring).

of clear and convincing evidence. *See, e.g.*, *The Barbed Wire Patent*, 143 U.S. 275, 284 (1892) (holding that testimony in patent cases is often "unsatisfactory" and requiring proof that is "clear, satisfactory, and beyond a reasonable doubt"); *Deering* v. *Winona Harvester Works*, 155 U.S. 286, 300, 301 (1894) ("grave suspicion" regarding testimony requires "evidence so cogent as to leave no reasonable doubt in the mind of the court that the transaction occurred substantially as stated"); *Trovan, Ltd.* v. *Sokymat SA*, 299 F.3d 1292, 1302 (Fed. Cir. 2002) ("To meet the clear and convincing burden of proof, alleged co-inventors must prove their contribution to the conception with more than their own testimony[.]"); *Price* v. *Symsek*, 988 F.2d 1187, 1194 (Fed. Cir. 1993) (claims to priority or derivation are "regarded with skepticism," so that "without some type of corroborating evidence, an alleged inventor's testimony cannot satisfy the 'clear and convincing evidence' standard"). Here, of course, Vanderbilt provided *no evidence*, let alone corroboration, of its theory that Dr. Daugan's invention of tadalafil was somehow influenced by the Vanderbilt professors' work with the IBMX analog.[3]

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[3] Vanderbilt states in a footnote that documentary evidence corroborated the Vanderbilt professors' discovery *of the IBMX analog*. Pet. 21 n.5. But the patents at issue do not claim the IBMX analog; rather, they claim *tadalafil* and other beta-carboline compounds. As the courts below held, *no* direct evidence corroborates Vanderbilt's speculation that its professors had *any* role whatsoever in Dr. Daugan's conception of the claimed beta-carboline compounds. Pet. App. 17a. Vanderbilt's failure to provide corroboration for its claims of co-inventorship provides an independent basis for affirmance, further counseling against a grant of review.

To be sure, the opinions below framed Vanderbilt's failure of proof in terms of a lack of "clear and convincing evidence" (Pet. App. 23a, 82a n.53), but that is understandable in light of the precedent that bound both courts. *E.g.*, *Hess* v. *Advanced Cardiovascular Sys., Inc.*, 106 F.3d 976, 979-980 (Fed. Cir. 1997). Nevertheless, the finding that the evidence regarding the identification of GR30040x was in equipoise would manifestly compel the same conclusion under a preponderance standard.

Vanderbilt has precious little to say about the effect of the finding that its theory was only "equally plausible" compared to ICOS's account (Pet. App. 82a)—other than to contend that the district court's finding was error, supposedly because the court failed to consider certain evidence (Pet. 10). But the court of appeals implicitly rejected that argument when it complimented the district court for its "thorough review of all of the evidence." *Id.* 18a; *see also id.* 23a (citing the district court's "careful review of the evidence"). Whether the district court did or did not consider particular evidence—and whether the court of appeals correctly found no error—is a case-specific factual determination that does not warrant this Court's review. *See* S. Ct. R. 10 (certiorari is "rarely granted" when the petition asserts "erroneous factual findings"); *United States* v. *Johnston*, 268 U.S. 220, 227 (1925) (Holmes, J.) ("We do not grant a certiorari to review evidence and discuss specific facts."). Certiorari is particularly unwarranted where, as here, "the findings of fact made by the district court receive the concurrence of the court of appeals." Gressman, § 4.14, at 271; *see also Berenyi* v. *District Dir., INS*, 385 U.S. 630, 635 (1967) (following the "Court's repeated pronouncements" against reviewing factual findings that were "reached by the Dis-

trict Judge and accepted by the Court of Appeals"); *Graver Tank & Mfg. Co.* v. *Linde Air Prods. Co.*, 336 U.S. 271, 275 (1949) ("A court of law, such as this Court is, rather than a court for correction of errors in fact finding, cannot undertake to review concurrent findings of fact by two courts below in the absence of a very obvious and exceptional showing of error.").

Vanderbilt also claims that the district court "found that Vanderbilt's scientists contributed *to the process* through which Dr. Daugan invented the compounds." Pet. 11 (emphasis added) (citing Pet. App. 80a). But a contribution to the "inventive process" (Pet. App. 80a) is not the same as a contribution to the conception of the invention itself. *See, e.g.*, *Ethicon, Inc.* v. *U.S. Surgical Corp.*, 135 F.3d 1456, 1460 (Fed. Cir. 1998) ("Because conception is the touchstone of inventorship, each joint inventor must generally contribute to the conception of the invention." (alteration and internal quotation marks omitted)). The district court accordingly cited a case that expressly distinguished between significant "contributions to conception" on the one hand and "prosaic contributions to *the inventive process* that do not render the contributor a co-inventor" on the other. *Eli Lilly & Co.* v. *Aradigm Corp.*, 376 F.3d 1352, 1359 (Fed. Cir. 2004) (emphasis added) (cited at Pet. App. 80a). The court specifically ruled that the Vanderbilt scientists' contributions to Dr. Daugan's "inventive process," if any, were of the second "'prosaic'" kind. Pet. App. 80a. Indeed, the parties agreed that Dr. Daugan, and Dr. Daugan alone, conceived tadalafil and the other claimed compounds. *Id.* 23a.

Moreover, as the court of appeals correctly ruled, the district court's ultimate finding, reviewing the evidence in full, was that even Vanderbilt's theory as to the identification of GR30040x—which was at most a

"prosaic" step in Dr. Daugan's "inventive process," not itself an inventive contribution—was itself no more than "equally plausible." Pet. App. 23a, 82a. The panel majority ruled that the principal finding that the parties' accounts were "equally plausible" compelled a finding that Vanderbilt failed to carry its burden—a determination that would stand under a preponderance test as well. Vanderbilt may well disagree with that view, but the interpretation of a particular trial court opinion in a particular case does not warrant this Court's intervention.

Vanderbilt has no other path to relief in this case. The panel was unanimous—and Vanderbilt does not seriously dispute—that there was *no* evidence (let alone a preponderance) that the Vanderbilt professors collaborated with Dr. Daugan himself, which would have required an "open line of communication during ... [the named inventor's] inventive efforts," *Cook Biotech Inc.* v. *ACell, Inc.*, 460 F.3d 1365, 1373 (Fed. Cir. 2006) (internal quotation marks omitted), as well as "some element of joint behavior." *Kimberly-Clark Corp.* v. *Procter & Gamble Distrib. Co.*, 973 F.2d 911, 917 (Fed. Cir. 1992) ("Individuals cannot be joint inventors if they are completely ignorant of what each other has done[.]"). As the court of appeals noted, there was no evidence of any collaboration here. Pet. App. 16a-19a; *see also id.* 26a (Dyk, J., concurring in part and dissenting in part) (agreeing with panel majority in upholding the district court's finding that Dr. Daugan "did not himself directly utilize" the Vanderbilt professors' work). And Vanderbilt does not dispute that disclosure to a company like Glaxo is insufficient to establish disclosure to an individual inventor. *See Beall* v. *Ormsby*, 154 F.2d 663, 665-666 (C.C.P.A. 1946).

Thus, Vanderbilt's only route to success was to prove (1) that Dr. Labaudinière searched for and found GR30040x based on his knowledge of Vanderbilt's IBMX analog and (2) that the identification of GR30040x was in fact an inventive (and not a "prosaic") contribution to the conception of tadalafil. But as the court of appeals found, Vanderbilt's case failed on the first point. There was "no clear error in the district court's factual findings underpinning its determination regarding Glaxo's identification of GR30040x" (Pet. App. 18a), given Vanderbilt's failure to offer anything more than attorney argument to support its claim in the face of "direct evidence supporting Dr. Labaudiniere's claim to sole identification of GR30040x" (*id.* 17a). Even viewing ICOS's evidence with skepticism, the district court found that Vanderbilt's case did not surpass "equal[]" plausibility. *Id.* 82a. And on the key question whether the Vanderbilt scientists "communicated to Glaxo a compound of the general structure of [the compounds] of the patents at issue," Vanderbilt's presentation was "devoid of evidence." *Id.* 79a. Thus, Vanderbilt's claim was properly rejected no matter what standard of proof applied.

As is discussed in the following section, the Court should not reassess the settled standard of proof applicable in correction-of-inventorship cases under Section 256. But even if the Court were interested in embarking on such a venture, this case is not a suitable vehicle for it. Merits review in this case would be a moot court that would unnecessarily squander Court and party resources. If the issue is as important as Vanderbilt in-

sists it is, the Court can await a case in which it might actually make a difference.[4]

B. Even If This Case Were A Suitable Vehicle, The Clear-And-Convincing-Evidence Standard For Correction-Of-Inventorship Claims Would Not Merit Review

Even if Vanderbilt's Section 256 claim could succeed under a preponderance standard—and it cannot—the Federal Circuit's decades-long jurisprudence that such claims require clear and convincing evidence is correct and should not be upset. The Court should therefore decline to review the issue, just as it has before. Pet. for Cert. 12, *D.S. Brown Co.* v. *Acme Highway Prods. Corp.*, No. 70-1140 (U.S. Dec. 21, 1970) (contending that the court of appeals "erred ... in its ruling that joint inventorship must be proven by clear and convincing evidence"), *cert. denied*, 401 U.S. 956 (1971).

Vanderbilt's primary argument for certiorari in this case is that claims under Section 256 are exactly the same as all other civil claims. Pet. 21. But Section 256 was not enacted in a vacuum. Rather, it was part of

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[4] Vanderbilt is wrong to suggest (Pet. 22-23) that an error regarding the standard of proof can never be harmless. *See, e.g.*, *Bowoto* v. *Chevron Corp.*, 621 F.3d 1116, 1124 (9th Cir. 2010) (affirming where "any difference in the burden of proof" would be "immaterial under the circumstances of this case"). Indeed, courts of appeals have affirmed even where the district court has placed the burden on the wrong *party*. *E.g.*, *Barth* v. *Gelb*, 2 F.3d 1180, 1189 (D.C. Cir. 1993) ("Viewing the evidence through the lens of those findings, we conclude that it was not so closely balanced that the court's error in assigning the burden of persuasion to Mr. Barth would have affected the outcome."); *Cates* v. *Morgan Portable Bldg. Corp.*, 780 F.2d 683, 688 (7th Cir. 1985) ("The judge's error about who had the burden of proof was harmless.").

the 1952 Patent Act, which—among other things—codified several preexisting patent law doctrines. *E.g.*, Lutz, *The New 1952 Patent Statute*, 35 J. Pat. Off. Soc'y 155, 156 (1953) ("Congress ... codified some doctrines of patent law that were developed in the courts by 'common law' processes."). The requirement of clear and convincing evidence predated the 1952 Act by at least three years. *See Pointer* v. *Six Wheel Corp.*, 177 F.2d 153, 157 (9th Cir. 1949) ("[I]t must appear by clear and convincing proof that the two inventors collaborated in evolving the patented device."). Congress is presumed to legislate on the background of that doctrine—a principle Vanderbilt does not appear to contest with respect to the requirement of independent corroboration of inventorship evidence. Pet. 20-21; *see Abuelhawa* v. *United States*, 129 S. Ct. 2102, 2106 (2009) ("legislatures act with case law in mind," so that Congress is presumed to be familiar with "traditional judicial" approaches); *Beck* v. *Prupis*, 529 U.S. 494, 501 (2000) (Congress "presumably knows and adopts the cluster of ideas that were attached" to statutory terms, so that the "absence of contrary direction may be taken as satisfaction with widely accepted definitions, not as a departure from them" (internal quotation marks omitted)); *North Star Steel Co.* v. *Thomas*, 515 U.S. 29, 34 (1995) ("'[I]t is not only appropriate but also realistic to presume that Congress was thoroughly familiar with [our] precedents ... and that it expect[s] its enactments to be interpreted in conformity with them.'" (quoting *Cannon* v. *University of Chi.*, 441 U.S. 677, 699 (1979)).[5]

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[5] *Accord, e.g.*, *Merck & Co.* v. *Reynolds*, 130 S. Ct. 1784, 1795 (2010) (citing cases); *Miles* v. *Apex Marine Corp.*, 498 U.S. 19, 32

Decisions in several circuits have articulated the clear-and-convincing standard under the 1952 Act,[6] yet Congress has never sought to alter that settled requirement, despite remaining "'free to alter what [courts] have done.'" *Watson* v. *United States*, 552 U.S. 74, 82 (2007). In 1984, Congress amended the definition of a joint inventor in Section 116, expressly referencing lower court decisions. Pet. App. 10a (noting that the 1984 amendments codified the principles of *Monsanto Co.* v. *Kamp*, 269 F. Supp. 818 (D.D.C. 1967)). Those amendments made it easier to become a joint inventor, by recognizing for example joint inventors who did not physically work together, but Congress elected not to relax the uniformly-applied standard of proof in correction-of-inventorship cases. "The responsibility for changing [settled law] rests with Congress," *Festo Corp.* v. *Shoketsu Kinzoku Kogyo Kabushiki Co.*, 535

(1990) (Congress "must have intended to incorporate" the established judicial "gloss" because "Congress is aware of existing law when it passes legislation"); *Goodyear Atomic Corp.* v. *Miller*, 486 U.S. 174, 184-185 (1988) ("We generally presume that Congress is knowledgeable about existing law pertinent to the legislation it enacts."); *T.I.M.E. Inc.* v. *United States*, 359 U.S. 464, 474 (1959) (Supreme Court "cannot assume [Congress] was unaware" of a common law decision relevant to its establishment of a statutory scheme).

[6] *E.g.*, *Hess*, 106 F.3d at 980; *Acme Highway Prods. Corp.* v. *D.S. Brown Co.*, 431 F.2d 1074, 1083 (6th Cir. 1970) ("[I]t has been well established that joint inventorship must be proven by clear and convincing evidence."); *Garrett Corp.* v. *United States*, 422 F.2d 874, 880 (Ct. Cl. 1970) ("The burden of showing misjoinder or nonjoinder of inventors is a heavy one and must be proved by clear and convincing evidence"); *see also Levin* v. *Septodont Inc.*, 34 F. App'x 65, 70 (4th Cir. 2002) (party seeking to correct patent's list of inventors "must prove that claim by clear and convincing evidence").

U.S. 722, 739 (2002), and Congress has declined to make the change that Vanderbilt seeks.[7]

In its supplemental brief, Vanderbilt belatedly attempts to liken its case to *i4i*, which involves the applicability of a clear-and-convincing-evidence standard in invalidity challenges based on prior art not placed before the Patent Office. *See* Pet. for Cert. i, *Microsoft Corp.* v. *i4i Ltd. P'ship*, No. 10-290 (U.S. Aug. 27, 2010). But as Vanderbilt recognizes, eleven amicus briefs supported Microsoft's petition for certiorari, emphasizing the claimed frequency with which the standard of proof may be dispositive in invalidity cases. By contrast, not one amicus has supported Vanderbilt's petition in this case or even suggested that it raises a question of significant importance. As shown in the preceding section, even *this case* does not turn on the issue.[8]

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[7] Clear and convincing evidence is additionally appropriate because claims under 35 U.S.C. § 256 are equitable in nature, *Shum* v. *Intel Corp.*, 499 F.3d 1272, 1277 (Fed. Cir. 2007), and plaintiffs seeking equitable relief have historically had to prove factual contentions by clear and convincing evidence. *See* 2 *McCormick on Evidence* § 340 & n.15, at 488 (6th ed. 2006) (citing cases). In fact, one authoritative commentator has questioned whether Section 256 creates an independent cause of action at all, given that the statutory language does not purport to do so. *See* 1 *Chisum on Patents* § 2.04[7], at 2-142 (Nov. 2007) (finding the existence of federal jurisdiction under Section 256 "highly questionable, both in terms of the statutory language of Section 256 and of policy").

[8] Although the use of a clear-and-convincing standard to prove co-inventorship has been linked to the presumption of validity, *see, e.g.*, *Stern* v. *Trustees of Columbia Univ. in City of N.Y.*, 434 F.3d 1375, 1377 (Fed. Cir. 2006), the standard is supported by other "important policy considerations"—most notably countering the temptation for aspiring co-inventors to reconstruct their prior

* * *

No matter how *4i* is resolved, the outcome in this case will be the same, because Vanderbilt failed to prove that its professors are entitled to be named co-inventors by even a preponderance, and clear and convincing evidence is a longstanding common law standard that Congress has implicitly approved and never disturbed. There is no need, and certainly no pressing need, for this Court to review Vanderbilt's first question presented.

II. An Appellate Court's Authority To Affirm On An Alternative Ground Supported By The Record Is Settled, Particularly Where The District Court Has Made The Necessary Supporting Findings

Vanderbilt's second question presented is almost an afterthought, and understandably so: it attempts to discard a settled doctrine that this Court and every circuit have articulated countless times, namely that an appellate court "may affirm on any ground that the law and the record permit." *Thigpen* v. *Roberts*, 468 U.S. 27, 30 (1984); *see also, e.g.*, *Jaffke* v. *Dunham*, 352 U.S. 280, 281 (1957) (per curiam) ("A successful party in the

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state of mind and inflate their contributions, "particularly where, as here, the patent has been outstanding for a considerable time and the patented device has been successful." *Hess*, 106 F.3d at 980 (citing *Amax Fly Ash Corp.* v. *United States*, 514 F.2d 1041, 1047 (Ct. Cl. 1975)). These considerations have particular force in this case, where scientists came forward years after the patents issued to assert—without evidence—joint inventorship of a highly successful commercial product.

District Court may sustain its judgment on any ground that finds support in the record.").[9]

Here, the Federal Circuit's affirmance was all the more justified because it rested on a basis that *the district court itself accepted.* As the panel majority explained, the district court "did not rest its opinion solely" on the interpretation of the law of inventorship that the Federal Circuit held erroneous. Pet. App. 23a. Rather, the district court—like the Federal Circuit—*separately* ruled that Vanderbilt failed to carry its burden to show that its professors contributed to the conception of the claimed compounds, because its speculative theory of events regarding the identification of the unclaimed GR30040x compound was only "equally plausible" when compared to ICOS's evidence. *Id.* 23a, 82a. That finding sufficed to support the judgment, and the Federal Circuit was fully entitled to affirm on that basis notwithstanding disagreeing with the district court's alternative ground of decision. *See, e.g.*, *Morgan Stanley Capital Group Inc.* v. *Public Util. Dist. No. 1 of Snohomish County*, 128 S. Ct. 2733, 2749 (2008) (affirming "on alternative grounds," despite "significant disagreement" with the lower court); *Siegert* v. *Gilley*,

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[9] *Accord Carreras* v. *Sajo, Garcia & Partners*, 596 F.3d 25, 36 (1st Cir. 2010); *Shelton* v. *Kennedy Funding, Inc.*, 622 F.3d 943, 952 (8th Cir. 2010); *Friends of Tims Ford* v. *TVA*, 585 F.3d 955, 964 n.2 (6th Cir. 2009); *Brooks* v. *Ross*, 578 F.3d 574, 578 (7th Cir. 2009); *Berquist* v. *Washington Mut. Bank*, 500 F.3d 344, 349 (5th Cir. 2007); *United States* v. *Smith*, 395 F.2d 516, 519 (4th Cir. 2005); *Davis* v. *Roberts*, 425 F.3d 830, 834 (10th Cir. 2005); *Green* v. *CSX Transp., Inc.*, 414 F.3d 758, 765 (7th Cir. 2005); *Koziara* v. *City of Casselberry*, 392 F.3d 1302, 1306 n.2 (11th Cir. 2004); *ACEquip Ltd.* v. *American Eng'g Corp.*, 315 F.3d 151, 155 (2d Cir. 2003); *Serrano* v. *Francis*, 345 F.3d 1071, 1076-1077 (9th Cir. 2003); *Tourscher* v. *McCullough*, 184 F.3d 236, 240 (3d Cir. 1999).

500 U.S. 226, 234-235 (1991) (affirming even though the court of appeals misread precedent, because "[b]y a different line of reasoning, we reach the same conclusion").

The alternative ground of decision, which is supported by the evidence and findings of record, amply distinguishes this case from *Pullman-Standard* v. *Swint*, 456 U.S. 273 (1982). As Vanderbilt acknowledges, the district court in *Pullman-Standard* had *failed* to make findings on a matter that the Fifth Circuit held was legally relevant (a union's intent in an employment discrimination suit). Rather than remand to allow the district court "to make the missing findings," the Fifth Circuit made those findings itself, set aside the district court's factual finding of no discriminatory intent, and *reversed* the district court's decision. *Id.* at 275, 282-284, 291. This Court disapproved that practice because Federal Rule of Civil Procedure 52(a) "requires that findings of fact not be set aside unless clearly erroneous." *Id.* at 287; *see also id.* at 293. While a remand is indeed preferable where, as in *Pullman-Swint* and the other cases Vanderbilt cites, the court of appeals' reversal on a legal issue implicates factual matters on which no finding was made,[10] those rulings do

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[10] *See Impax Labs., Inc.* v. *Aventis Pharms. Inc.*, 468 F.3d 1366, 1383 (Fed. Cir. 2006) (remanding for a determination that had "not yet been done," because "the district court stopped its analysis"); *Trovan*, 299 F.3d at 1310 (remanding because the district court "did not completely address" claim construction issues); *W.L. Gore & Assocs., Inc.* v. *Garlock, Inc.*, 721 F.2d 1540, 1547 (Fed. Cir. 1983) ("the invention set forth in each claim was not in each instance considered as a whole," and "the references were not assessed in their entireties"); *see also United States* v. *Hasan*, 609 F.3d 1121, 1129 (10th Cir. 2010) (remanding where district court

not speak to this case, where the court of appeals affirmed on an alternative ground that remains unaffected by the legal ruling.

Here, the Federal Circuit did not make any new findings, set aside findings made by the district court, or reverse the district court's judgment. Rather, it *affirmed* on a ground that the trial court itself articulated and supported with its finding that Vanderbilt failed to carry its burden of proof (even by a preponderance). Thus, this is not a case in which the court of appeals "attempt[ed] to reach its own factual findings" or "usurp[ed] ... a trial court's role in weighing evidence against the appropriate legal standard." Pet. 25. Rather, the district court's finding of evidentiary equipoise was independent of its approach to inventorship law, and the panel majority *affirmed* that finding as based on "a careful review of the evidence." Pet. App. 23a. That finding compelled affirmance, even under Vanderbilt's desired standard of proof.[11]

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failed to undertake the first step in a "two-step, sequential inquiry").

Notably, three of the four cases Vanderbilt cites as applying the correct rule are from the Federal Circuit, which suggests either that Vanderbilt's supposed conflict does not exist or that it may be resolved by further percolation within the Federal Circuit.

[11] Since Vanderbilt's second question is presented independently of its first, it is properly considered on the basis that the Federal Circuit and district court correctly applied the clear-and-convincing-evidence standard. But even if a preponderance standard applied, the district court's findings still compel the same result. *See supra* Part I.A.

CONCLUSION

The petition for a writ of certiorari should be denied.

Respectfully submitted.

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No. 10-412

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In The Supreme Court of The United States

VANDERBILT UNIVERSITY,
Petitioner,

v.

ICOS CORPORATION,
Respondent.

ON PETITION FOR WRIT OF CERTIORARI
TO THE UNITED STATES COURT OF APPEALS
FOR THE FEDERAL CIRCUIT

SUPPLEMENTAL BRIEF

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Newegg, Inc., Pregis Corporation, Public Knowledge, Computer & Communications Industry Association, SAP America, Inc., Securities Industry and Financial Markets Association, TEVA Pharmaceuticals USA, Inc., Toyota Motor Corporation, Trimble Navigation Limited, Verizon Communications Inc., Wal-Mart Stores, Inc., Yahoo!, Inc., and thirty-six other law and economics professors filed eleven briefs *amicus curiae* in support of a petition for writ of certiorari filed by Microsoft Corporation in *Microsoft Corp. v. I4I Limited Partnership, et al.*, No. 10-290. Those briefs revealed that there is broad support across a number of significant industries for the uniform application of the preponderance of evidence burden of proof to civil actions under the Patent Act. These eleven briefs filed by fifty-four *amici* apply with equal force to Vanderbilt's Petition for Writ of Certiorari; indeed, it would be inconsistent for the Court to grant Microsoft Corporation's petition without granting Vanderbilt's Petition.

Microsoft Corp. v. I4I Limited Partnership addresses the Federal Circuit's imposition of a clear and convincing burden of proof in the context of an invalidity claim under Section 282 of the Patent Act, 35 U.S.C. §282. The basis upon which the Federal Circuit has imposed that higher burden in Section 282 cases, and which is attacked by the Microsoft *amici*, is the presumption of validity extended to patents. This is the identical justification used by the Federal Circuit for imposing the heightened burden of proof in Section 256 cases, which is the focus of Vanderbilt's petition. *Hess v. Adv. Cardio. Sys., Inc.*, 106 F.3d 976, 980 (Fed. Cir. 1997). Thus,

if the Supreme Court were to grant Microsoft's petition and rule in *Microsoft Corporation v. I4I Limited Partnership* that the burden for proving invalidity is preponderance of the evidence, such a holding would eviscerate any justification for imposing the higher clear and convincing standard upon Section 256 cases. Therefore, it is in the interest of justice that the Court considers the Vanderbilt petition in conjunction with the Court's consideration of the Microsoft petition.

Respectfully submitted this 13TH day of October, 2010,

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RULE 29.6 STATEMENT

The Corporate Disclosure Statement included in the Petition for a Writ of Certiorari remains accurate.

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REPLY BRIEF FOR PETITIONER

ICOS acknowledges that the Federal Circuit's imposition of a clear-and-convincing-evidence standard on Section 256 actions arises from that court's imposition of that standard on Section 282 invalidity claims. Opp. 24, n.8. This Court has recognized that the imposition of that heightened standard, where there is no evidence that Congress intended such a standard, is an important issue worthy of this Court's review. *See Microsoft Corp. v. i4i Limited Partnership* (No. 10-290). Confronted with this fact, ICOS devotes the majority of its opposition to an evidentiary argument that the imposition of a preponderance-of-evidence standard could not possibly affect the outcome of Vanderbilt's claim; an argument made possible only by ICOS' mischaracterization of the District Court's findings and failure to acknowledge the contrary view of the Court of Appeals. ICOS' fallback position---that Congress codified a pre-existing clear-and-convincing-evidence standard for actions to correct the inventors on a patent in the Patent Act of 1952---is wrong and disingenuous. No such cause of action existed prior to the Act.

The Court should grant Vanderbilt's petition for the same reasons raised in *Microsoft* as Vanderbilt's case is actually a better vehicle for the Court to consider the burden of proof issue. If the Court does not grant Vanderbilt's petition outright the Court should hold Vanderbilt's petition pending a decision in *Microsoft* because that decision is likely to impact the outcome of Vanderbilt's case. Acknowledging that possibility, ICOS suggests that the Court could reasonably establish a rule in *Microsoft* that the preponderance-

of-evidence standard applies to all claims of invalidity, or even just those based upon information not considered by the PTO, but retain a higher clear-and-convincing-evidence standard in Section 256 cases. Opp. 2, 3, 13, 24-25. If that was the case an accused infringer would have a lesser burden *to invalidate a patent* by proving that a patent failed to list a joint inventor than the misjoined or unnamed inventor would have in a claim *to preserve the patent's validity* through correction under Section 256. The absurdity of such a result is obvious. If the standard changes for Section 282 it must change for Section 256.

I. THE STANDARD OF PROOF ISSUE RAISED IN VANDERBILT'S PETITION IS WORTHY OF REVIEW BY THIS COURT

A. Vanderbilt Has Raised an Important Issue of Law

As this Court has noted, "[b]ecause the Federal Circuit has exclusive jurisdiction over appeals from all United States District Courts in patent litigation," when that Court repeatedly misconstrues some aspect of the law in that area "it is a matter of special importance to the entire Nation" that warrants this Court's review notwithstanding a lack of conflicting decisions from other circuits. *Cardinal Chem. Co. v. Morton Int'l, Inc.*, 508 U.S. 83, 89 (1993).[1] This is true

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[1] The imposition of the clear-and-convincing evidence standard on Section 256 claims is arguably in conflict with pre-1982 opinions from other circuits that preponderance of the evidence was the appropriate burden in the invalidity context. *See Manufacturing Research Corp. v. Graybar Electric Co.*, 679 F.2d 1355, 1360-61

where the Federal Circuit imposes a rule on a section of the Patent Act inconsistent with Congress' intent as reflected in the text. *Pfaff v. Wells Electronics, Inc.* 525 U.S. 55, 60 (1998). Section 256 makes no reference to the heightened clear-and-convincing-evidence burden of proof imposed by the Court of Appeals. Thus, even if Vanderbilt's petition was limited to the issue of whether the Court of Appeals erred in imposing that burden, the petition should be granted.

ICOS concedes that neither the text nor legislative history of Section 256 reflect a Congressional intent to impose a heightened burden on parties seeking to correct a patent. However, ICOS asserts that prior to the passage of the Patent Act of 1952 courts had established a clear-and-convincing-evidence standard in such cases and that Congress intended to codify that standard into Section 256. Opp. 21. Quite the contrary, Section 256 created an entirely new cause of action.

The Patent Act of 1952 only "partly" codified the common law of patents that had evolved prior to that time. Karl B. Lutz, *The New 1952 Patent Statute*, 35 J. Pat. & Trademark Off. Soc'y 156, 157 (1953). Entitled "An Act *to revise* and codify the laws relating to patents and the Patent Office, and to enact into law Title 35 of the United States Code entitled, 'Patents,'" (emphasis added), it also made "liberalizing changes."

(11th Cir. 1982); *Baumstimler v. Rankin*, 677 F.2d 1061, 1066 (5th Cir. 1982); *Futorian Mfg. Corp. v. Dual Mfg. & Eng'g. Inc.*, 528 F.2d 941, 943 (1st Cir. 1976).

See also P.J. Federico, *Commentary on the New Patent Act*, 75 J. Pat. & Trademark Off. Soc'y 161, 170 (1993) (reprinting commentary to 35 U.S.C. § 1 et seq. (West 1954). One of the "more important" liberalizing changes was Section 256. Lutz, *supra*, at 162. *See also* Frederico, *supra*, at 210 ("Section 256 ... is entirely new.")

Before 1952, a finding that a patent that did not accurately identify inventors could only result in voiding the patent. *MCV, Inc. v. King-Seeley Thermos Co.*, 870 F.2d 1568, 1570 (Fed. Cir. 1989). Thus, prior to the 1952 Act, the *only* purpose for proving joint inventorship in court was to invalidate a patent.[2] Section 256 was enacted to change that common law and preserve patents from invalidity.

> Section 256 is a new section in the law that is correlated with section 116 and relates to a mistake in joining a person as a joint inventor. Very often two or three people make an invention together. They must apply as joint inventors. If they make a mistake in determining who are the true inventors, they do so at their

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[2] *See Pointer v. Six Wheel Corp.*, 177 F.2d 153 (9th Cir. 1949) cited by ICOS as evidence that court's imposed a clear-and-convincing-evidence burden on actions to correct patents prior to the 1952 Act. Opp. at 22. Pointer, accused of infringement, sought to prove joint inventorship for the purpose of invalidating the patent. Likewise the defendant in *Acme Highway Products Corp. v. D.S. Brown Co.*, 431 F.2d 1074 (6th Cir. 1970), whom ICOS suggests unsuccessfully petitioned this Court to review the imposition of a clear-and-convincing-evidence burden on Section 256 claims. Opp. 21.

> peril. This provision permits a bona fide mistake in joining a person as inventor or in failing to join a person as an inventor to be corrected.
>
> S. Rep. No. 1979, 82d Cong., 2d Sess., p. 7 (1952).

Iowa State Research Foundation, Inc. v. Sperry Rand Corp., 444 F.2d 406, 408 (4th Cir. 1971) (footnotes omitted). *See also In re Richard N. Bennett*, 766 F.2d 524 (Fed. Cir. 1985) (legislative history of this provision makes clear its remedial intent).

As Congress clearly intended in Section 256 to depart from existing law to preserve patents, there is no basis for concluding that Congress nonetheless intended to impose the heightened burden of proof previously imposed upon parties seeking to invalidate patents. In enacting Section 256 Congress presumably was aware that the burden generally imposed in civil actions is the preponderance-of-the-evidence standard and its silence on the issue suggests that Congress intended that standard be applied. *Grogan v. Garner*, 478 U.S. 279, 286 (1991); *Herman & MacLean v. Huddleston, et al.*, 459 U.S. 375, 390 (1983); *Price Waterhouse v. Hopkins*, 490 U.S. 228, 253 (1989). *See also Abuelhawa v. U.S.*, 129 S. Ct. 2102, 2106 (2009) (legislature is presumed to act with case law in mind). Moreover, because a patent cannot be invalidated through a Section 256 claim, Congress clearly intended a preponderance-of-evidence standard be applied to Section 256 regardless of whether a heightened standard is imposed on infringers seeking to invalidate

patents under Section 282.

The Federal Circuit has repeatedly been asked and has refused to rectify its error with respect to the burden of proof imposed on Section 256 claims.[3] As the question is unlikely to reach any other circuit, only this Court can correct that error. *Pfaff*, 525 U.S. at 60. If this Court fails to address this issue, the continued uncertainty with respect to the appropriate burden will generate unnecessary costs for future Section 256 claimants, opponents, and the courts.

B. Only the District Court Can Determine if the Application of the Preponderance-of-Evidence Standard Will Change the Outcome of Vanderbilt's Claims

ICOS repeatedly argues that the District Court found that it was "equally plausible" that the Vanderbilt scientists did or did not contribute to the conception of the claimed compounds, such that Vanderbilt would not have prevailed even under a preponderance-of-evidence standard. Opp. *passim*. ICOS misrepresents the District Court's findings.

As discussed in the Petition, as part of its case Vanderbilt argued that the evidence showed that the identification of the compound GR30040X was the result of a database search using the structure of the

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[3] ICOS' corporate parent asked the Court of Appeals to correct this error in the context where parallel interference proceedings are pending. *Eli Lilly v. Aradigm Corp.*, 376 F.3d 1352 (Fed. Cir. 2004).

Vanderbilt scientists' novel PDE V inhibitor. Pet. 9-10. That evidence included an English translation of meeting minutes that were inconsistent with ICOS' competing assertion that GR30040X was identified through a search using another compound. Pet. 10.[4] Holding Vanderbilt to a clear-and-convincing-evidence standard, and expressly failing to consider the meeting minutes, the trial court found that the parties' competing assertions with respect to how GR30040X was identified were "equally plausible." Pet. 10; Pet. App. 81a-82a, ¶91. The District Court *never* found that it was only plausible that the Vanderbilt scientists had contributed to the invention. The District Court found that the Vanderbilt scientists contributed and that ICOS' arguments to the contrary were "untenable." Pet. App. 80a, ¶88. *See also* Pet. App. 30a.

Although finding that the District Court erroneously applied a standard for joint invention that required all joint inventors to conceive of the entire claimed invention, the Court of Appeals affirmed the District Court's conclusion that Vanderbilt had failed to prove its claim under a clear-and-convincing-

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[4] At trial ICOS abandoned the story that ICOS and Glaxo had espoused as to how GR30040X was identified, after Vanderbilt proved the story false. Pet. App. 61a – 63a, ¶¶60-64; 70a, ¶¶71-72. ICOS concedes that the October 1992 meeting minutes were inconsistent with ICOS' new story and that an English translation was in evidence. ICOS concedes that the **very first** modification to GR30040X included replacement of the pyridine ring with a phenyl ring **and** electron donating methoxy substituent to create GF173321X, consistent with incorporating the Vanderbilt structure, resulting in significantly increased potency as a PDE V inhibitor, and that further development of GF173321X, not any other attempted GR30040X variations, led to the claimed compounds. Pet. 7-8.

evidence standard. As to whether the outcome would have been different had the District Court applied a preponderance-of-evidence standard, the Court of Appeals stated:

> We express no view on whether Vanderbilt would prevail under a preponderance of the evidence test. Vanderbilt is of course free to seek *en banc* reconsideration of our settled law on this issue.

(App. at 17a-18a, n. 3). Remarkably, ICOS fails to address this statement. Vanderbilt submits that the Court of Appeals would not invite a petition for rehearing if it was clear on the record that the outcome of Vanderbilt's claim would be unchanged under a preponderance-of-evidence standard. That determination should be left to the District Court on remand.

C. Vanderbilt's Case Is the Ideal Vehicle to Resolve the Burden of Proof Issue

Vanderbilt asserted that the preponderance-of-evidence standard should apply to Section 256 before, during, and after trial, and preserved that argument in its appeal and its petition for rehearing. As the Court of Appeals observed, there is clearly a question whether the District Court, applying the preponderance-of-evidence standard and the appropriate test for joint inventorship, would find in favor of Vanderbilt. Thus, Vanderbilt's case is an excellent vehicle for this Court to consider whether the preponderance-of-evidence standard should be applied to Section 256.

Vanderbilt framed its first issue broadly as to whether it is *ever* appropriate for a court to impose a heightened burden of proof on a statutory civil action when there is no evidence Congress intended such a burden. Thus, if the Court grants Vanderbilt's petition the Court's review could extend beyond Section 256 and encompass claims of patent invalidity under Section 282, which the Court has already deemed worthy of review in *Microsoft*. There a number of advantages to the Court reviewing the issue through Vanderbilt's case than through *Microsoft*:

- i4i Limited Partnership has raised issues as to whether Microsoft sufficiently preserved the issue for appeal to this Court.

- The day after the conference in which the Court considered the *Microsoft* petition, the PTO concluded that the prior art references submitted by Microsoft did not create a "substantial new question of patentability," raising questions whether a decision by the Court in *Microsoft* will impact the outcome of that case.

- The Chief Justice recused himself from participating in *Microsoft*, creating a possibility of a split decision.

Vanderbilt's case suffers from none of these potential problems and, therefore, presents a vehicle that is more likely to resolve the burden of proof controversy.

D. A Decision in Favor of the Petitioner in *Microsoft* Will Necessarily Impact Vanderbilt's Case

Even if the Court holds in *Microsoft* that the clear-and-convincing-evidence standard *should* apply to invalidity claims asserted under Section 282, that holding would not control Vanderbilt's case. Validity cannot be attacked through Section 256. Thus the presumption of validity provides no basis for not applying the preponderance-of-evidence standard typically imposed in civil actions. The lower standard is far more consistent with the presumption of validity and Congress' remedial intention that Section 256 claims preserve the validity of patents.

On the other hand, if the Court holds in *Microsoft* that the preponderance-of-evidence standard should be applied to invalidity claims, even if only where the asserted invalidity rests on information not before the PTO, that result will require that a similar burden apply in Section 256 cases. An infringer may assert invalidity under § 282(2) because the applicant "did not himself invent the subject matter sought to be patented" as required under 35 U.S.C. § 102(f). Applicants are not required to submit evidence that they are the only and true inventors, and ICOS stipulated that the PTO undertakes no effort to verify the identity of inventors. Thus, if the Court adopts Microsoft's position, regardless of the rule the Court fashions, alleged infringers asserting invalidity based upon of a failure to list a joint inventor will always have their claims judged against a preponderance-of-evidence standard. Under those circumstances, continued imposition of a clear-and-convincing-

evidence standard on Section 256 claims would be absurd. The idea that it should be harder for a joint inventor to correct and preserve the validity of a patent under Section 256 than for an infringer to invalidate a patent under Section 282 simply cannot be reconciled with the language and legislative history of Section 256 nor the presumption of validity.

The Court should grant Vanderbilt's petition as it is the only means by which the Federal Circuit's error with respect to Section 256 can be rectified. At a minimum, the Court should hold Vanderbilt's petition pending a ruling in *Microsoft* so as to avoid an absurd and unjust result.

II. THE COURT OF APPEALS' FAILURE TO REMAND TO THE DISTRICT COURT IS WORTHY OF REVIEW BY THIS COURT

ICOS' opposition to Vanderbilt's petition with respect to the Court of Appeals' failure to remand is comprised of (1) string cites for the proposition that a Court of Appeals can affirm a District Court on any grounds found in the record; and (2) a rehashing of evidentiary arguments as to why the Court of Appeals might have affirmed the District Court's judgment under a clear-and-convincing-evidence standard. It misses the point of Vanderbilt's argument and this Court's holding in *Pullman-Standard v. Swint*, 456 U.S. 273 (1982). When the District Court considers the evidentiary record against a significantly flawed legal standard, all of the District Court's resulting factual findings become suspect. A Court of Appeals should not ignore the risk that those findings were tainted by the District Court's error and simply apply the correct

legal standard to those "infirm" findings. It should remand the case to the District Court "for further proceedings to permit the trial court to make the missing findings," because "where findings are infirm because of an erroneous view of the law, a remand is the proper course unless the record permits only one resolution of the factual issue." *Pullman-Standard*, 456 U.S. at 291-92.

If the Court wishes to be inundated with the parties' competing evidentiary arguments those can be presented in detail through the briefs and appendix.[5] At this juncture, the important and incontestable points are fairly simple. The District Court measured the evidence against a rule that required a joint inventor to contribute **the entire invention**. The District Court found that the Vanderbilt scientists made a contribution, but as it was not the whole invention, it did not constitute joint invention and thus need not be defined. As Judge Dyk pointed out in his dissent, it was impossible for the remaining members of the panel to apply the appropriate standard to the Vanderbilt contributions. The majority simply ignored those contributions. That may have made it easy for the majority to conclude that there was only one resolution, but it is not the method this Court intended in *Pullman-Standard*. The Court should grant Vanderbilt's petition and review whether the Court of Appeals acted in accordance with that law.

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[5] These will include references to the evidence showing that Vanderbilt's contributions were provided to Dr. Labaudinière, who, in turn, directed Dr. Daugan's work on GR30040X, and that Dr. Daugan was provided extensive portions of the Vanderbilt's scientists' research without any attribution of its source or notice to Vanderbilt.

CONCLUSION

Vanderbilt's petition for writ of certiorari should be granted.

Respectfully submitted this 30TH day of December, 2010,

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